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RICHTER'S ORGANIC CHEMISTRY
or
THE CHEMISTRY OF THE CARBON COMPOUNDS

RICHTER-ANSCHÜTZ:
THE CHEMISTRY OF THE CARBON COMPOUNDS

Volume One: —THE ALIPHATIC SERIES
Volume Two: —THE ALICYCLIC COMPOUNDS AND NATURAL PRODUCTS
Volume Three: —THE AROMATIC COMPOUNDS
Volume Four:—THE HETEROCYCLIC COMPOUNDS AND ORGANIC FREE RADICALS

ORGANIC CHEMISTRY

OR

CHEMISTRY OF THE CARBON COMPOUNDS

BY

VICTOR VON RICHTER

EDITED BY

PROF. RICHARD ANSCHÜTZ AND DR. FRITZ REINDEL

VOLUME I

CHEMISTRY OF THE ALIPHATIC SERIES

NEWLY TRANSLATED AND REVISED FROM THE 12TH GERMAN EDITION
(AFTER THE TRANSLATION OF THE 2ND ENGLISH EDITION
BY PERCY E. SPIELMANN, PH.D., B.SC., F.I.C., A.R.C.SC.)

BY

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PREFACE TO THE THIRD ENGLISH EDITION

This is the sixth edition in the English language of Richter's "Organic Chemistry," three American Editions preceding the first English one. It follows 15 years after the first English Edition and includes all the new and revised matter of the 12th German Edition, and a good deal of further matter which it was felt desirable to insert.

The arrangement of the matter in the introduction is a characteristic feature of the book, which has been preserved in this edition. It is realized that with the great advances which are now taking place on the theoretical side of organic chemistry, some subjects may appear inadequately dealt with, and in places the presentation may appear somewhat old-fashioned, but without entirely rewriting and rearranging the introductory section, which would entirely alter the individuality of the book, this is largely inevitable. Short articles on the Electronic Theory of Valency and the Parachor have, however, been included, on account of their importance in the understanding of some problems of a stereochemical and constitutional nature.

It was suggested in several reviews of the last edition that the replacement of the numerous "Centralblatt" references by their originals was desirable. This has been done as regards the majority of the references from 1910 onwards: in addition, a number of further references have been included.

Many minor amendments and additions have been made throughout the book.

In matter of nomenclature, where the English and German usage varies, English custom has been followed. Thus the substance originally described as 'γ-glucose' is referred to as glucofuranose rather than heteroglucose. The use of Greek letters for indicating position in open chains has been continued with the exception of sugar derivatives, where the use of arabic numerals has become more or less universal.

My thanks are due to Dr. W. H. Hurtley, who kindly read certain portions of the manuscript, and to the publishers and printers for their co-operation in producing a very difficult piece of typography.

ABBREVIATIONS

JOURNALS

Am. Chem. J.	American Chemical Journal.
Ann.	Liebig's Annalen der Chemie.
Ann. Chim.	Annales de Chimie.
Ann. Chim. Phys.	Annales de Chimie et de Physique.
Ber.	Berichte der deutschen chemischen Gesellschaft.
Biochem. J.	Biochemical Journal.
Biochem. Z.	Biochemische Zeitschrift.
Bull. Soc. Chim.	Bulletin de la Société chimique de Paris.
C.	Chemisches Centralblatt.
Compt. rend.	Comptes rendus des Séances de l'Academie des Sciences.
Chem. News	Chemical News.
Chem. Ztg.	Chemiker-Zeitung.
Gazzetta	Gazzetta chimica italiana.
J.A.C.S.	Journal of the American Chemical Society.
J.C.S.	Journal of the Chemical Society.
J. pr. Chem.	Journal für praktische Chemie.
J.S.C.I.	Journal of the Society of Chemical Industry.
Monatsh.	Monatshefte für Chemie.
Phys. Zeitsch.	Physikalische Zeitschrift.
Pogg. Ann.	Annalen der Physik und Chemie (Poggendorf): New series (Wiedemann).
Wied. Ann.	See Pogg. Ann.
Z. anal. Chem.	Zeitschrift für analytische Chemie.
Z. angew. Chem.	Zeitschrift für angewandte Chemie.
Z. anorg. Chem.	Zeitschrift für anorganische Chemie.
Z. Electroch.	Zeitschrift für Electrochemie.
Z. physik. Chem.	Zeitschrift für physikalische Chemie.
Z. physiol. Chem.	Zeitschrift für physiologische Chemie (Hoppe-Seyler).

OTHER IMPORTANT ABBREVIATIONS

Ac.	Acetyl (CH_3CO).
b.p.	Boiling-point.
D.	Density.
Et.	Ethyl (C_2H_5).
Me.	Methyl (CH_3).
m.p.	Melting-point.
(+) and (−)	indicate direction of rotation of an optically active compound, irrespective of its stereochemical relationships.
$[\alpha]$	Specific optical rotatory power.

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A TEXT-BOOK

OF

ORGANIC CHEMISTRY

INTRODUCTION

WHILST *inorganic chemistry* was developed primarily through the investigation of minerals, and was in consequence termed *mineral chemistry*, it may be said that the development of *organic chemistry* was due to the study of products resulting from the alteration of plant and animal substances. About the close of the eighteenth century Lavoisier demonstrated that, when the organic substances present in vegetable and animal organisms were burned, carbon dioxide and water were always formed. He also showed that the component elements of these bodies, so different in properties, were generally carbon, hydrogen, oxygen, and, especially in animal substances, nitrogen. Lavoisier further gave utterance to the opinion that peculiarly constituted atomic groups, or radicals, were to be accepted as present in organic substances; whilst the mineral substances were regarded by him as the direct combinations of single elements.

As it seemed impossible, for a long time, to prepare organic bodies synthetically from the elements, the opinion prevailed that there existed an essential difference between organic and inorganic substances, which led to the use of the names *Organic Chemistry* and *Inorganic Chemistry*. The prevalent opinion was, that the chemical elements in the living bodies were subject to other laws than those in the so-called inanimate nature, and that the organic substances were formed in the organism only by the intervention of a peculiar vital force, and that they could not possibly be prepared in an artificial way.

One fact sufficed to prove these views to be unfounded. The first organic substance artificially prepared was urea (*Wöhler*, 1828). By this synthesis chiefly, to which others were soon added, the idea of a peculiar force necessary to the formation of organic compounds was contradicted. All further attempts to separate organic substances from the inorganic (the chemistry of the simple and the chemistry of the compound radicals, p. 21) were futile. At present we know that these do not differ essentially from each other; that the peculiarities of organic compounds are dependent solely on the nature of their essential constituent, Carbon; and that all substances belonging to plants and animals can be prepared artificially from the elements. Organic Chemistry is, therefore, the *chemistry of the carbon compounds.* Its separation from the chemistry of the other elements is necessitated only by practical considerations, on account of the very great number of carbon compounds (about 180,000 : see M. M. Richter's Lexikon der Kohlenstoffverbindungen : Annual increase, some 5000 new compounds), which far exceeds those of all other elements put together. No other possesses in the same degree the ability of the carbon atoms to unite with one another to form open and closed rings or chains. The numerous existing carbon nuclei in which atoms or atomic groups of other elements have entered in the formation of organic derivatives have arisen in this manner.

The impetus given to the study of the compounds of carbon has not only brought new industries into existence, but it has caused the rapid development of others of like importance to the growth and welfare of the nation.

The advances of organic chemistry are equally important to the investigation of the chemical processes in vegetable and animal organisms, a section of the subject known as *Physiological Chemistry* or *Biochemistry.*

DETERMINATION OF THE COMPOSITION OF CARBON COMPOUNDS

ELEMENTARY ORGANIC ANALYSIS

Most carbon compounds occurring in the animal and vegetable kingdoms consist of carbon, hydrogen, and oxygen, as was demonstrated by Lavoisier, the founder of organic elementary analysis. Many, also, contain nitrogen, whilst sulphur and phosphorus are often present. Almost all the elements, non-metals and metals, may be artificially introduced as constituents of carbon compounds in direct union with carbon. The number of known carbon compounds is exceedingly great. A general method, therefore, of isolating the several compounds of a mixture, as is done in inorganic chemistry in the separation of bases from acids, is impracticable, and special methods have to be devised.* The task of elementary organic analysis is to determine, qualitatively and quantitatively, the elements of a carbon compound after it has been obtained in a pure state and characterized by definite physical properties, such as crystalline form, specific gravity, melting point, and boiling point. Simple practical methods for the direct determination of oxygen do not exist ; its quantity is usually calculated by difference, after the other constituents have been found.

DETERMINATION OF CARBON AND HYDROGEN

The presence of carbon in a substance is shown by its charring when ignited out of contact with air. In general its quantity, as also that of the hydrogen, is ascertained by combustion. The substance is mixed in a glass tube with copper oxide and heated, or the vapour of the

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* Systematic separation of mixtures of carbon compounds, see *H. Staudinger,* Anleitung zur organischen qualitativen Analyse (Berlin, 1923, Springer).

substance is passed over red-hot copper oxide. The cupric oxide gives up its oxygen and is reduced to metallic copper, whilst the carbon burns to carbon dioxide, and the hydrogen to water. In quantitative analysis, these products are collected separately in special apparatus, and the increase in the weight of the latter determined. Carbon and hydrogen are always simultaneously determined in one operation. The details of the quantitative analysis are fully described in the text-books of analytical chemistry.* It is only necessary here, therefore, to outline the methods employed. Liebig's name is especially associated with the elaboration of these methods (Pogg. Ann. 1831, **21**, 1).

Usually the combustion is effected by the aid of copper oxide or fused and granulated lead chromate in a tube of hard glass, fifty to seventy centimetres long (depending upon the greater or less volatility of the organic body). Substances which burn with difficulty should be mixed with finely divided cupric oxide, finely divided lead chromate, or with cupric oxide to which potassium bichromate has been added, or the combustion is carried out in a stream of oxygen. (Use of moist oxygen, see Ber. **46**, 949.)

The tube is usually open at both ends (*Glaser*, Ann. Suppl. **7**, 213) but Liebig employed a tube drawn to a point. For many reasons tubes of fused silica are preferable (*cf.* Ber. **41**, 604 : Ann. **358**, 232). An iron tube has also been used (*Cloëz*, Z. anal. Chem. **2**, 413).

The tube is placed in a suitable furnace, charcoal being originally used as a heating agent, but gas or electrical heating (see Ber. **39**, 2263) is usually employed. A particularly economical gas furnace was devised by Frerichs and Normann (Z. angew. Chem. **29**, 367 (1916)), the tube being enclosed by large slabs of kieselguhr of special shape. (Early references, *A. W. Hofmann*, Ann. **90**, 235 : **107**, 37 : *Erlenmeyer sen.*, Ann. **139**, 70 : *Glaser*, *loc. cit.* : *Anschütz* and *Kekulé*, Ann. **228**, 301 : Fuchs, Ber. **25**, 2723.)

When the tube has been filled, the open end is attached to an apparatus designed to collect the water produced in the combustion. The substances used to retain the moisture are :

1. A U-tube filled with carefully purified calcium chloride, which has been dried at 180° C.

2. Pure, concentrated sulphuric acid contained in a specially designed tube, or pumice fragments, dipped in the acid, and placed in a U-tube (*Mathesius*, Z. anal. Chem. **23**, 345).

3. Pellets of glacial phosphoric acid, contained in a U-tube. The vessel intended to receive the water is in air-tight connection with the apparatus designed to absorb the carbon dioxide. For the latter purpose a Liebig potash bulb was formerly employed, but later that of Geissler came into use ; and very many other forms have been recommended (Ber. **24**, 271 : C. 1900, I. 1240). U-tubes, filled with granulated soda-lime, are substituted for the customary bulbs (*Mulder*, Z. anal. Chem. **1**, 2).

When the combustion is finished, oxygen free from carbon dioxide is forced into or drawn through the combustion-tube, air being substituted for it later, with the precaution that the pieces of apparatus serving to dry the oxygen and air are filled with the same material which was used for absorbing the water produced by the combustion. As soon as the entire system is filled with air, the pieces of apparatus employed for absorbing the water and carbon dioxide are disconnected and weighed separately. The increase in weight of the apparatus in which the water is collected represents the water resulting from the combustion of the weighed substance, and the increase in the other the quantity of carbon dioxide. Knowing the composition of water and carbon dioxide the quantity of carbon

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* *J. Liebig*, Anleitung zur Analyse organischer Körper, 2. Aufl. 1853 : *R. Fresenius*, Quantitative chemische Analyse, 6. Aufl., Bd. 2 : *Vortmann*, Chemische Analyse organischer Stoffe : *M. Dennstedt*, Die Entwicklung der organischen Elementaranalyse, 1899 : *Meyer*, Analyse und Konstitutionsermittelung organischer Verbindungen, 4. Aufl. (Springer, 1922) : *Houben*, Die Methoden der organischen Chemie, Bd. I, S. 20–96 (Leipzig, 1921, Thieme).

and hydrogen contained in the burnt substance can readily be calculated in percentage.

Fig. 1 represents one end of a combustion furnace of the type devised by Kekulé and Anschütz (Ann. **228**, 301). In it lies the combustion tube *V*. This is connected with a Klinger calcium chloride tube, *A* ; *B* is a Geissler potash-bulb, joined to a U-tube, *C*, one limb of which is filled with pieces of stick potash, and the other with calcium chloride. *G* represents mica plates, which permit of a careful observation of the flame. *E* is a section of the iron tube (Modification, C. 1903, I. 609) in which the combustion tube *V* rests ; *T* a side clay cover placed over the mica strips ; *D* a clay cover for the top. *R* is the gutter into which the gas-pipe, bearing the burners, is placed, and from which it can be removed for repair, etc.

Fig. 1 also shows, above the combustion tube, the anterior portion of a similar tube V^1, provided with a Bredt and Posth (Ann. **285**, 385) calcium chloride tube A^1, in which the movement of a drop of water enables the analyst to determine the rapidity of the combustion. B^1 is a U-tube filled with soda-lime and provided with ground-glass stoppers. C^1 is a similar tube, filled one-half with soda-lime and one-half with calcium chloride.

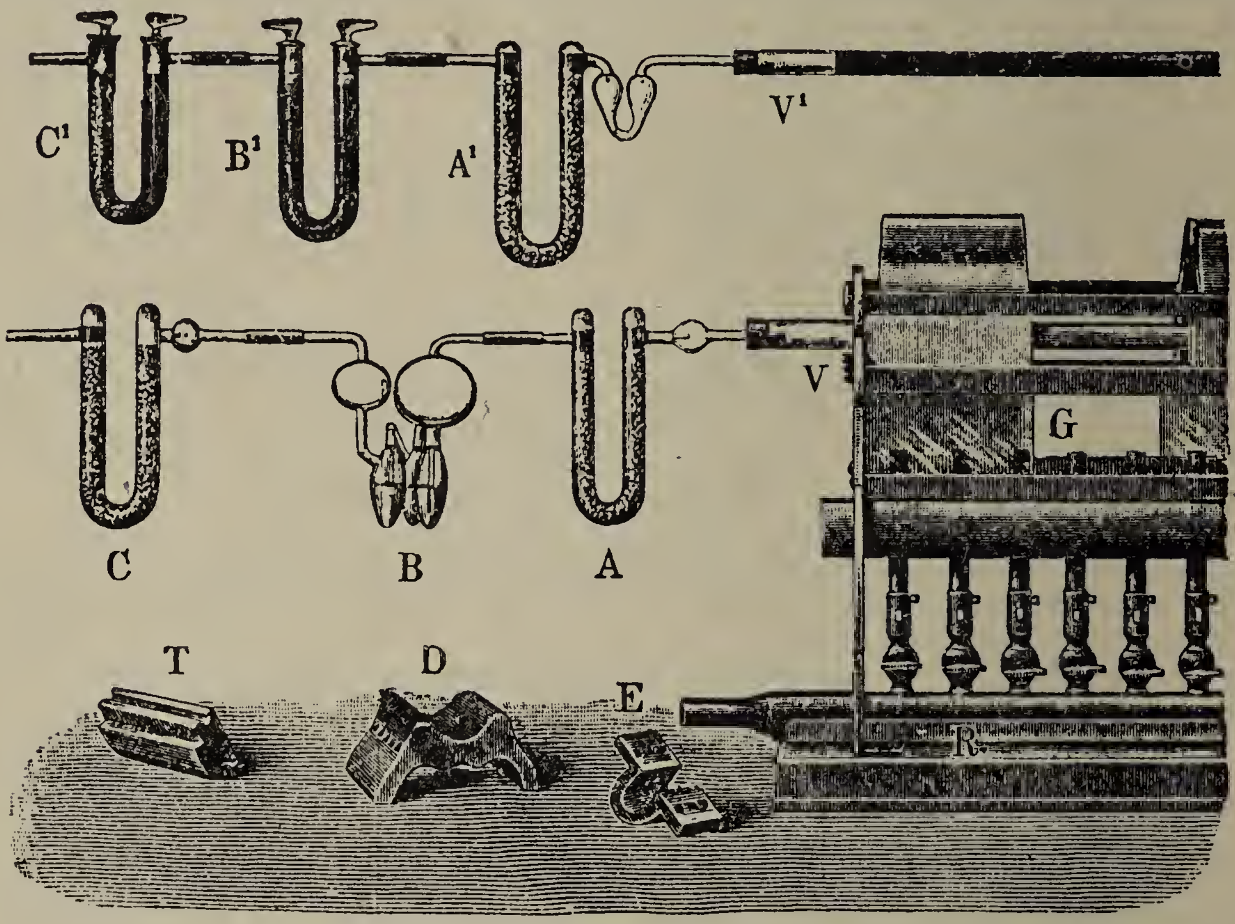

Fig. 1.

Instead of oxidizing the organic substance with the combined oxygen of cupric oxide or lead chromate, the method of Kopfer may be employed, in which platinum black is made to carry free oxygen to the vapours of the substance. A simpler combustion furnace may then be employed.

This method has been perfected by Dennstedt * and his co-workers. In his "rapid combustion method" the substance is introduced into a small tube and vaporized therefrom into a slow stream of oxygen. At the same time a more rapid current of the gas is sent round the small containing tube and over the heated contact substance (platinized quartz, thin strips of platinum foil or platinum gauze), so that the vapour of the compound to be combusted is always in the presence of a large excess of oxygen. The accompanying illustration (Fig. 2) indicates clearly the arrangement (Ber. **38**, 3729 : **39**, 1623 : **41**, 600 : Chem. Ztg. **33**, 769).

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* *Dennstedt,* Anleitung zur vereinfachten Elementar-analyse, 3. Aufl. **Hamburg, 1910.**

Cerium dioxide has been used as a contact substance (Ber. **46**, 2574).

Hempel and others have worked out methods for the combustion of solid organic substances with oxygen under pressure in the autoclave (Ber. **30**, 202, 380, 605).

Gaseous bodies can be analysed according to the usual gas analysis methods, either with Bunsen's * apparatus, or with Hempel's,† when great accuracy is not required. The volume of the gas or mixture of gases is measured after each successive reaction with potassium hydroxide solution, fuming sulphuric acid, alkaline pyrogallic acid and ammoniacal cuprous chloride. These reagents absorb respectively carbon dioxide, the so-called heavy hydrocarbons (olefines, acetylene, aromatic hydrocarbons of the C_nH_{2n-6} series), oxygen and carbon monoxide. The gaseous residue, which may consist of nitrogen, hydrogen and methane, is either exploded with oxygen and the contraction in volume measured both before and after absorption of the carbon dioxide formed ; or else the two combustible gases may be separately dealt with, the hydrogen being absorbed by palladium black and the methane being led over incandescent platinum. A complete separation of the ethylene hydrocarbons from those of the benzene series has been successfully carried out by the employment of activated charcoal (*Berl*, Z. angew. Chem. **34**, 125 : **37**, 205 : Chem. Ztg. **50**, 332).

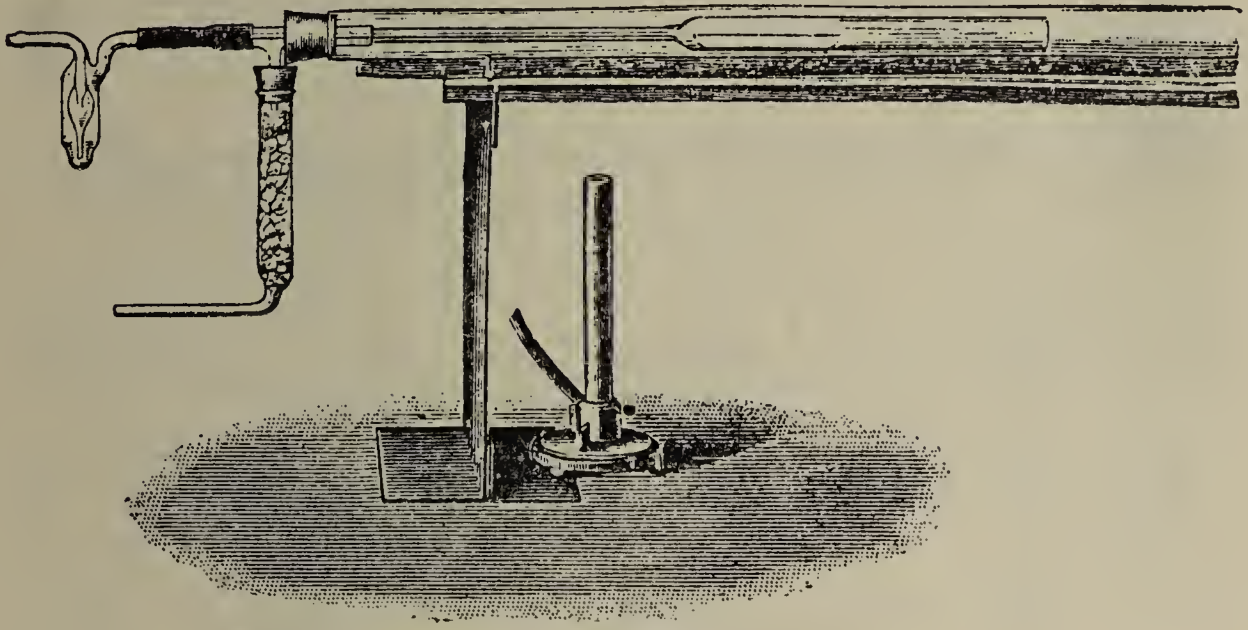

Fig. 2.

When **nitrogen** is present in the substances burned, its oxides are sometimes produced, which have to be reduced to nitrogen. This may be effected by conducting the gases of the combustion over a layer of metallic copper filings, or a roll of copper gauze placed in the front portion of the combustion tube. The latter, in such cases, should be a little longer than usual. The copper, which has been previously reduced in a current of hydrogen, often includes some of the gas which, on subsequent combustion, would yield water. To remedy this, the copper after reduction is heated in an air-bath or, better, in a current of carbon dioxide or to 200° in a vacuum. Its reduction by the vapours of formic acid or methyl alcohol is more advantageous ; this may be done by pouring a small quantity of these liquids into a dry test tube and then suspending in them the roll of copper heated to redness ; copper thus reduced is perfectly free from hydrogen.

It is generally unnecessary to use a copper spiral when the combustions are carried out in open tubes.

If the substance contains **chlorine, bromine** or **iodine**, copper halides are formed, which, being volatile, would pass into the calcium chloride tube. In order to avoid this a spiral of thin copper, or better, silver foil is introduced into the front part of the tube. When the organic compound contains **sulphur**

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* *Bunsen*, Gasometrische Methoden, 2. Aufl. Braunschweig, 1877.

† *Hempel*, Gasometrische Methoden, Braunschweig, 1913 : *Winkler*, Gasanalyze, Freiberg, 1901 : *Zsigmondy und Jander*, Kurzer Leitfaden der technischen Gasanalyse, Vieweg, Braunschweig, 1920.

a portion of the latter will be converted into sulphur dioxide (during the combustion with cupric oxide), which may be prevented from escaping by introducing a layer of lead peroxide (Z. anal. Chem. **17**, 1). Or lead chromate may be substituted for the cupric oxide, which would convert the sulphur into non-volatile lead sulphate. In the combustion of organic salts of the alkalis or alkaline earths, a portion of the carbon dioxide is retained by the base. To prevent this and to expel the CO_2, the substance in the boat is mixed with potassium bichromate or chromic oxide (Ber. **13**, 1641).

An organic substance, containing nitrogen, sulphur, chlorine or bromine, can be analysed by Dennstedt's method (see above, Fig. 1). It is mixed with lead peroxide and placed in a boat of special shape in the front part of the tube. The temperature is then raised to about 320°. The nitrogen, sulphur, and halogens are held back in the form of lead compounds, whilst the carbon and hydrogen pass away as carbon dioxide and water, and are estimated in the usual way.

When carbon alone is to be determined this can be effected, in many instances, in the wet way, by oxidation with chromic acid and sulphuric acid (*Messinger*, Ber. **21**, 2910 : compare Ann. **273**, 151 : Ber. **42**, 1305 : C. 1909, II. 2195 : Apparatus, Chem. Ztg. **97**, 917 (1912)).

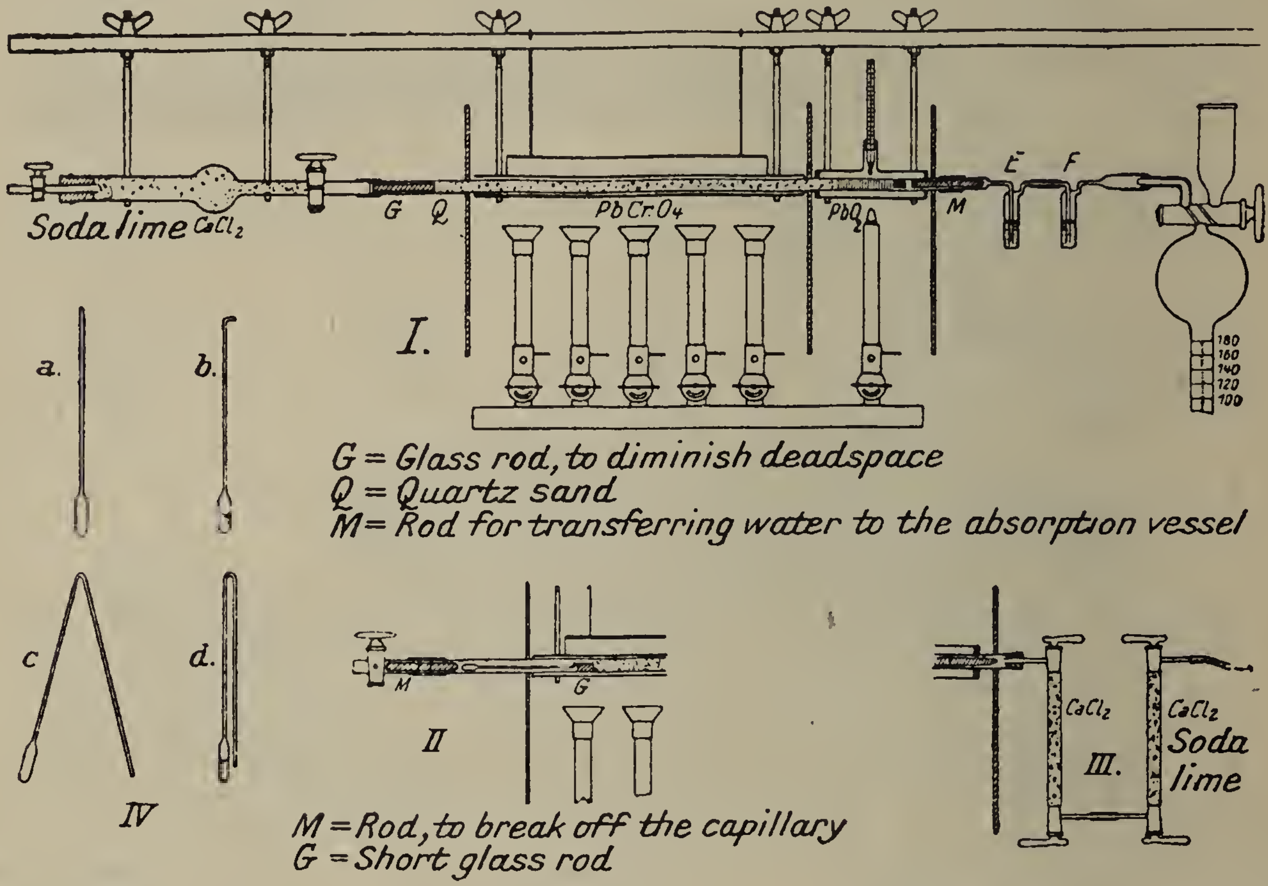

FIG. 3.

A method for the electric combustion of substances with platinum as catalyst is described in Chem. Ztg. **33**, 733.

The aim of the newer methods is the use of smaller quantities of substance to be analysed, a great saving of time being thereby obtained. Berl (Ber. **59**, 890 : **61**, 83) has worked out a rapid method for the estimation of carbon and hydrogen, whereby, using a quantity of substance containing up to 15 mg. carbon, the process can be carried through in 40–45 minutes. The apparatus is illustrated in Fig. 3.

The substance is oxidized by heating with finely powdered lead chromate, and the evolved carbon dioxide estimated either volumetrically (Fig. 3, I) or gravimetrically (Fig. 3, III). The water is in either case estimated as the increase in weight of the absorption vessels (conc. sulphuric acid, Fig. 3, I, *E* and *F*) or calcium chloride (Fig. 3, III). In the case of substances containing nitrogen, halogen or sulphur, a layer of lead peroxide is necessary before the absorption vessels. Liquids are weighed in the small vessels illustrated in Fig. 3, IV, which are placed for combustion as shown in Fig. 3, II.

The method necessitates burning at a known rate, and careful preparation of the reagents used for filling the tube and absorption vessels. Experimental details, see Ber. **61**, 83.

Microestimation of Carbon and Hydrogen

(*Pregl*, Die quantitative organische Mikroanalyse, 2. Aufl. Springer, Berlin, 1923 : *Dubsky*, Organische Mikroelementaranalyse : *Houben*, Arbeitsmethoden der organischen Chemie, Bd. I.)

The increase in the sensitivity of the analytical balance to 0·005–0·001 mg. (so-called microbalances, Kuhlmann, Bunge, Sartorius) has been used by Pregl for the development of microanalytical methods. The majority of elements can be estimated, using a quantity of 3–5 mg. of substance. The apparatus for the estimation of carbon and hydrogen is illustrated in Fig. 4. The filling of the combustion tube with silver wool, copper oxide and lead chromate, and lead peroxide enables the same tube to be used for substances containing nitrogen, halogen or sulphur. For details of this masterly method, the above works should be consulted.

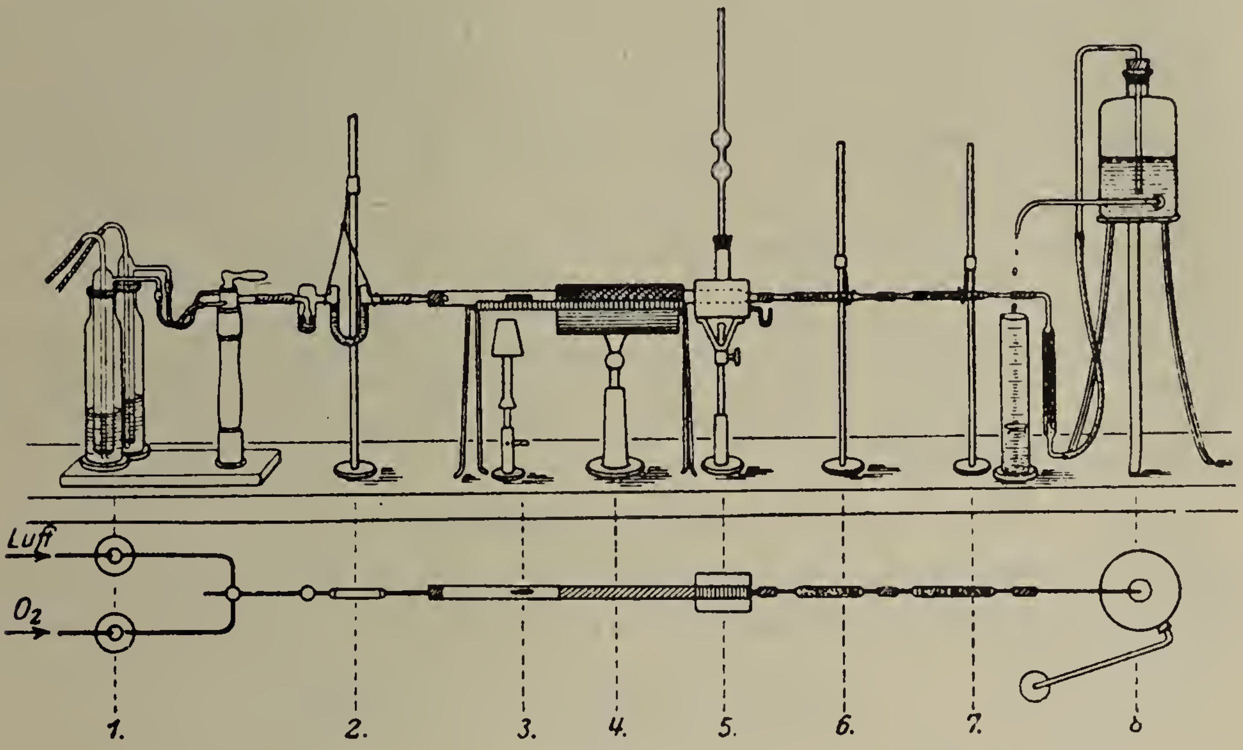

FIG. 4.

1. Pressure Regulator. 2. Bubble Counter. 3. Platinum Boat. 4. $CuO + PbCrO_4$. 5. Cymene bath, for heating PbO_2 to 180°. 6 and 7. Absorption apparatus for Cl_2O and CO_2. 8. Marriotte's Bottle.

DETERMINATION OF NITROGEN

In many instances, the presence of nitrogen is disclosed by the odour of burnt feathers when the compounds under examination are heated. Many nitrogenous substances yield ammonia when heated with alkalis (or, better still, with soda-lime). A simple and very delicate test for the detection of nitrogen is the following : the substance is heated in a test tube with a small piece of sodium or potassium, or, when the substance is explosive, with the addition of dry soda. Potassium cyanide is produced, accompanied perhaps by a slight detonation. The residue is treated with water ; to the filtrate, ferrous sulphate containing a ferric salt is added, and then a few drops of potassium hydroxide ; the mixture is then heated, and finally an excess of hydrochloric acid is added. An undissolved, blue-coloured precipitate (Prussian blue), or a bluish-green coloration, indicates the presence of nitrogen in the substance examined.

Nitrogen is determined quantitatively: (1) as nitrogen, by the method of *Dumas*; (2*a*) as ammonia, by the ignition of the material with soda-lime (method of *Will and Varrentrap*); (2*b*) as ammonia, by heating the substance with sulphuric acid according to the directions of *Kjeldahl.*

1. **Dumas' Method.**—The substance, mixed with cupric oxide, is burned in a tube of hard glass in the anterior end of which is a layer of metallic copper which serves for the reduction of the oxides of nitrogen. The tube is filled with carbon dioxide, obtained by heating either dry, primary sodium carbonate or magnesite, contained in the posterior and closed end of the tube. It can also be filled from a carbon dioxide apparatus of the type recommended by Kreusler (Z. anal. Chem. **24**, 440), in which case an open tube is used. A more practicable method of procedure consists in evacuating the tube, previous to the combustion, by means of an air-pump, and filling each time with carbon dioxide (Ann. **233**, 330, note); or the air may be removed by means of a mercury pump (Z. anal. Chem. **17**, 409).

When the combustion is ended, excess of carbon dioxide is employed to sweep all the nitrogen from the combustion tube into the graduated tube or nitrometer, which may have one of a variety of forms (*Zulkowsky*, Ann. **182**, 296: Ber. **13**, 1099: *Schwarz*, Ber. **13**, 771: *Ludwig*, Ber. **13**, 883: *H. Schiff*, Ber. **13**, 885: *Staedel*, Ber. **13**, 2243: *Groves*, Ber. **13**, 1341: *Ilinski*, Ber. **17**, 1348). The potassium hydroxide in the graduated vessel absorbs all the disengaged carbon dioxide, and only pure nitrogen remains.

Micro Dumas method, see *Pregl*, Die quantitative organische Mikroanalyse, 1923: Semi-micro method, *Berl*. Ber. **59**, 897.

Given the volume V_t of the gas, the barometric pressure p and the vapour-pressure s of the potassium hydroxide (*Wüllner*, Pogg. Ann. **103**, 529: **110**, 564) at the temperature t of the surrounding air, the volume V_0 at 0° and 760 mm. may be easily deduced:

$$V_0 = \frac{V_t(p - s)}{760\ (1 + 0{\cdot}003665t)}.$$

Multiply V_0 by 0·0012507, the weight of 1 c.c. of nitrogen at 0° and 760 mm., and the product will represent the weight in grams of the observed volume of nitrogen:

$$G = \frac{V_t(p - s)}{760\ (1 + 1{\cdot}003665t)} \times 0{\cdot}0012507$$

from which the percentage of nitrogen in the substance analysed can easily be calculated.

Instead of reducing the observed gas volume V, from the observed barometric pressure and the temperature at the time of the experiment, to the normal pressure of 760 mm. and the temperature of 0° ("N.T.P."), the reduction may be more readily effected by comparing the observed volume of gas or vapour with the expansion of a normal gas-volume (100) measured at 760 mm. and 0°. For this purpose the equation $V_0 = V.\frac{100}{v}$ is employed, in which v represents the changed normal volume (100). The gas-volumometer recommended by *Kreusler* (Ber. **17**, 30) and *Winkler* (Ber. **18**, 2534), or the *Lunge nitrometer* (Ber. **18**, 2030: **23**, 440: **24**, 1656, 3491: *J. A. Müller*, Ber. **26**, R. 388) will answer very well for this purpose. Or the nitrogen may be collected in a *gas-baroscope*, and its weight calculated from the pressure of a known constant volume of nitrogen (Ber. **27**, 2263).

Frankland and *Armstrong* conduct the combustion in a vacuum, and dispense with the layer of metallic copper in the anterior portion of the tube. If any nitric oxide is formed it is collected together with the nitrogen, and is subsequently removed by absorption (Ber. **22**, 3065).

Consult *Hempel* (Z. anal. Chem. **17**, 409); *E. Pfluger* (*ibid.*, **18**, 296); *Jannasch* and *V. Meyer* (Ann. **233**, 375); and *Dennstedt* and *Hassler* (Ber. **41**, 2778) for methods by which carbon, hydrogen, and nitrogen are determined simultaneously.

See *Gehrenbeck* (Ber. **22**, 1694) when nitrogen and hydrogen are to be estimated simultaneously, in cases where the carbon was determined in the wet way, as by *Messinger's* method.

For the simultaneous determination of carbon and nitrogen, see *Klingemann* (Ann. **275**, 92): *Frankland,* J.C.S. **99**, 1783.

2. **Will and Varrentrap's Method.**—When most nitrogenous organic compounds (nitro-derivatives excepted) are ignited with alkalis, all the nitrogen is eliminated in the form of ammonia gas. The weighed, finely pulverized substance is mixed with about 10 parts soda-lime, and placed in a combustion tube about 30 cm. in length, which is then filled with soda-lime. At the open end of the tube there is connected a bulb apparatus, containing dilute hydrochloric acid. The anterior portion of the tube in the furnace is first heated, then that containing the mixture. In order to carry all the ammonia into the bulb, air is passed through the tube, after the fused-up end has been broken. The ammonium chloride in the hydrochloric acid is precipitated with platinic chloride, as ammonium-platinum chloride ($PtCl_4,2NH_4Cl$); the precipitate is then ignited, and the residual Pt weighed; 1 atom of Pt corresponds to 2 molecules of NH_3 or 2 atoms of nitrogen.

Or, having employed a definite volume of acid in the apparatus, the excess after the ammonia absorption may be determined volumetrically, using fluorescein or methyl orange as an indicator.

Generally, too little nitrogen is obtained by this method, because a portion of the ammonia undergoes decomposition. This is avoided by adding sugar to the mixture of substance and soda-lime, and by avoiding heating the tube too strongly (Z. anal. Chem. **19**, 91). Further, the tube must be filled with soda-lime as completely as possible (Z. anal. Chem. **21**, 278).

The method of Will and Varrentrap is made more widely applicable by the addition of reducing substances to the soda-lime. *Goldberg* (Ber. **16**, 2549) recommends a mixture of soda-lime (100 parts), stannous sulphide (100 parts), and sulphur (20 parts); this he considers especially advantageous in estimating the nitrogen of nitro- and azo-compounds. For nitrates, *Arnold* (Ber. **18**, 806) employs a mixture of soda-lime (2 parts), sodium thiosulphate (1 part), and sodium formate (1 part).

3. **Kjeldahl's Method.**—The substance is dissolved by heating it with concentrated sulphuric acid. This decomposes the organic matter and converts the nitrogen into ammonia. After the liquid has been diluted with water and cooled and a small quantity of potassium permanganate has been added, the ammonia is expelled from it by boiling with sodium hydroxide (Z. anal. Chem. **22**, 366). This method is well adapted for the determination of the nitrogen of plants and animal substances (compare urea). When the nitrogen in nitro- and cyanogen compounds is to be estimated, sugar must be added; and in the case of nitrates, benzoic acid. The addition of mercury or copper sulphate is highly advantageous (Ber. **18**, R. 199, 297: **29**, R. 146). Pyridine and quinoline cannot be analysed by this method (Ber. **19**, R. 367, 368).

The Kjeldahl method for the determination of nitrogen has rapidly come into favour on account of the simplicity of the operation and of the apparatus, and of the possibility to carry out a number of determinations simultaneously. A large number of modifications of the method have been proposed to render it generally applicable (Ber. **27**, 1633: **28**, R. 937: C. 1898, II. 312).

Nitrogen as ·NO or ·NO₂.—The nitrogen of nitro- and nitroso-compounds can be determined indirectly with a standardized solution of stannous chloride. The latter converts the groups NO_2 and NO into the amide group, and is itself converted into an equivalent quantity of stannic chloride. This can be determined by titrating the excess of stannous salt with an iodine solution (*Limpricht,* Ber. **11**, 40).

The estimation of nitrogen in nitro groups can also be readily carried out by titration in acid solution with titanous sulphate (*Callan* and *Henderson,* J. Soc. Chem. Ind. 1922, **41**, 157–161 T), a modification of Knecht's titanous chloride method.

Estimation of nitrogen in amides, cyanides and proteins by titration with alkaline hypochlorite solution, see Ber. **37**, 4290.

DETERMINATION OF THE HALOGENS, SULPHUR, AND PHOSPHORUS

Qualitative Tests : *Halogens.*—Substances containing chlorine, bromine and iodine burn with a flame having a green-tinged border. The following reaction is exceedingly delicate. A little cupric oxide is first ignited on a platinum wire, then some of the substance to be examined is placed upon it, and the whole is heated in the non-luminous gas flame, which is coloured an intense greenish-blue if a halogen is present. A more definite test is to ignite the substance in a test tube with quick-lime (free from halogens), dissolve the mass in nitric acid, and then to add silver nitrate to the filtered solution.

Sulphur.—The presence of sulphur can frequently be detected by fusing the substance with potassium hydroxide ; potassium sulphide results, which produces a black stain of silver sulphide on a clean piece of silver ; or by heating the substance with metallic sodium and testing the aqueous filtrate for sodium sulphide with sodium nitroprusside : if sulphur is present, a purple-violet coloration is produced. When testing for sulphur and *phosphorus*, the substance is oxidized with a mixture of potassium nitrate and potassium carbonate ; the resulting sulphuric and phosphoric acids are sought for by the usual methods.

Quantitative Analysis : A hard glass tube, closed at one end, and about 33 cm. in length, containing a mixture of the substance with chlorine-free lime, is heated. After cooling, its contents are dissolved in dilute nitric acid, the solution is filtered and silver nitrate is added to precipitate the halogen.

The decomposition is easier if instead of lime a mixture of lime with $\frac{1}{4}$ part sodium carbonate, or 1 part sodium carbonate with 2 parts potassium nitrate is employed ; and in the case of substances volatilizing with difficulty, a platinum, porcelain or steel crucible, heated over a gas lamp, can be used (*Volhard*, Ann. **190**, 40 ; *Scheff*, Ann. **195**, 293). With compounds containing iodine, iodic acid may form, which, after solution of the mass, may be reduced by sulphurous acid. The volumetric method of *Volhard* (Ann. **190**, 1) for estimating halogens, employing ammonium thiocyanate as indicator, is strongly to be recommended in place of the customary gravimetric method.

The same decomposition can also be effected by ignition with iron, ferric oxide, and sodium carbonate (*E. Kopp*, Ber. **10**, 290).

The substances containing the halogens may also be burned in oxygen. The gases are conducted over platinized quartz sand, and the products collected in suitable solutions (*Zulkowsky*, Ber. **18**, R. 648).

The substances may be burned in a current of oxygen, and the products conducted through a layer of pure granular lime (or soda-lime) raised to a red heat. Later, the lime is dissolved in dilute nitric acid, and the halogens, the sulphuric acid and the phosphoric acid may then be estimated. *Arsenic* may be determined similarly (*Brügelmann*, Z. anal. Chem. **15**, 1 : **16**, 1). Sauer recommends collecting the sulphur dioxide, formed in the combustion of the substance, in hydrochloric acid containing bromine, in an alkaline bromine solution, or a sodium peroxide solution (Z. anal. Chem. **12**, 178 : Chem. Ztg. **34**, 417 : Z. angew. Chem. **26**, 503). See also the simultaneous estimation of halogens and sulphur in the presence of carbon and hydrogen, by Dennstedt's method (p. 4).

To determine *sulphur* and the *halogens* by the method suggested by *Klason* (Ber. **19**, 1910), the substance is oxidized in a current of oxygen charged with nitrous vapours, and the products of combustion are conducted over rolls of platinum foil. Consult *Poleck* (Z. anal. Chem. **22**, 171) for the estimation of the sulphur contained in coal gas.

A method of frequent use for the determination of the halogens, sulphur, and phosphorus in organic bodies is that of *Carius* (Z. anal. Chem. **1**, 240 : **4**, 451 : **10**, 103) : *Linnemann* (*ibid.* **11**, 325) ; *Obermeyer* (Ber. **20**, 2928).

The substance, weighed out in a small glass tube, is heated together with concentrated nitric acid and silver nitrate to 150–300° C. in a sealed tube, and the quantity of the resulting silver haloid (Ber. **28**, R. 478, 864), sulphuric acid, and phosphoric acid determined. The furnace of Babo (Ber. **13**, 1219) is especially adapted for heating the tubes. The results by this method are not always reliable (Ann. **223**, 184).

The following method is more generally applicable for the estimation of sulphur and the halogens : the substance is carefully heated in a nickel crucible with a mixture of sodium and potassium carbonates and sodium peroxide. After having been melted, the product of reaction is dissolved in water and acidified with hydrochloric acid containing bromine ; the sulphur is then precipitated as barium sulphate (cf. Ber. **28**, 427 : Chem. Ztg. **19**, 2040 : C. 1904, II. 1622, etc.)

The method is usable with slight modification for the estimation of halogen (*Pringsheim*, Ber. **41**, 4267 : Literature, see Chem. Ztg. **35**, 906).

In many instances, the halogens may be separated by the action of sodium amalgam on the aqueous solution of the substance, or by that of sodium on the alcoholic solution. The quantity of the resulting salt is determined in the filtered liquid (*Kekulé*, Ann. Suppl. **1**, 340 ; comp. C. 1905, I. 1273 : Ber. **39**, 4056).

Sulphur and phosphorus can often be estimated by the wet method. The oxidation is effected by means of potassium permanganate and alkali hydroxide, or with potassium bichromate and hydrochloric acid (*Messinger*, Ber. **21**, 2914).

Estimation of *fluorine*, see Gazzetta, **49**, II. 371.

ESTIMATION OF CERTAIN IMPORTANT ORGANIC GROUPS

Estimation of Methoxyl and Ethoxyl Groups.—This method is due to Zeisel (Monatsh. **6**, 989 : **7**, 704). The substance is heated with concentrated hydriodic acid (D 1·72), whereby methyl or ethyl iodide is formed. This is distilled off and after removal of free iodine by red phosphorus, is caught in alcoholic silver nitrate solution. The silver iodide formed is estimated by weighing. Apparatus, see Monatsh. **25**, 1213. *Micro-method, Pregl*, Die quantitative organische Mikroanalyse. Improvement, see Z. physiol. Chem. **163**, 141. Methyl and ethyl groups attached to nitrogen can be estimated by a similar method (Ber. **27**, 319 : Monatsh. **15**, 613 : **16**, 599 : **18**, 379). Micro-method, see *Pregl, loc. cit.*

Estimation of Active Hydrogen.—Substances containing " active hydrogen " (OH, SH, NH_2, NH groups, etc.) react in an anhydrous solvent (dry pyridine) with magnesium methyl iodide to yield methane quantitatively. This is estimated volumetrically (*Zerewitinoff*, Ber. **40**, 2023 : **41**, 2223). *Micro-method, Flaschenträger*, Z. physiol. Chem. **146**, 219 : *Marrian*, Biochem. J. **24**, 746.

Estimation of Acetyl Groups.—Monatsh. **18**, 859 : Ber. **38**, 3956 : Ann. **433**, 430, 230. *Micro-method*, Ann. **440**, 34. **Estimation of benzoyl groups**, Ann. **294**, 215 : Ber. **28**, 2965.

DETERMINATION OF THE MOLECULAR FORMULA

The results of elementary analysis are expressed as the percentage composition of the substance thus examined ; then follows the determination of the *molecular formula*.

We arrive at the simplest ratio in the number of elementary atoms contained in a compound, by dividing the percentage numbers by the respective atomic weights of the elements.

Thus, the analysis of lactic acid gave the following percentage composition:

Carbon	40·0	per cent.
Hydrogen	6·6	,,
Oxygen (by difference)	53·4	,,
	100·0	

Dividing these numbers by the corresponding atomic weights (C = 12, H = 1, O = 16), the following quotients are obtained:

$$\frac{40\cdot0}{12} = 3\cdot3 \qquad \frac{6\cdot6}{1} = 6\cdot6 \qquad \frac{53\cdot4}{16} = 3\cdot3$$

Therefore, the ratio of the number of atoms of C, H, and O, in lactic acid, is as 3·3 : 6·6 : 3·3, or 1 : 2 : 1. The simplest atomic formula, then, would be CH_2O; however, it remains undetermined what multiple, if any, of this formula expresses the true composition. The lowest formula of a compound, by which is expressed the ratio of the atoms of other elements to those of the carbon atoms, is an *empirical formula*. We are actually acquainted with different substances having the empirical formula CH_2O, for example, formaldehyde, CH_2O; acetic acid, $C_2H_4O_2$; lactic acid, $C_3H_6O_3$; dextrose, $C_6H_{12}O_6$, etc.

With compounds of complicated structure, various empirical formulæ may be calculated from the percentage composition, on account of the possible errors of observation.

The true molecular formula, therefore, can only be ascertained by some other means. Three courses of procedure are open to us. First, the study of the chemical reactions, and the derivatives of the substance under consideration; second, the determination of the vapour density of volatile substances; and third, the examination of certain properties of the solutions of soluble substances.

(1) *Determination of the Molecular Weight by the Chemical Method*

This is applicable to all substances, but does not invariably lead to definite conclusions. It consists in preparing derivatives, analysing them and comparing their formulæ with the supposed formula of the original compound. The problem becomes simpler when the substance is either a base or an acid. Then it is only necessary to prepare a salt, determine the quantity of metal combined with the acid, or of the mineral acid in union with the base, and from this to calculate the equivalent formula. A few examples will serve to illustrate this.

The silver salt of lactic acid may be prepared (the silver salts are easily obtained pure, and generally crystallize without water) and the quantity of silver in it determined; 54·8 per cent. of silver will be found. As the atomic weight of silver = 107·7, the amount of the other constituent combined with one atom of Ag in silver lactate, may be calculated from the proportion—

$$54\cdot8 : (100 - 54\cdot8) :: 107\cdot7 : x$$
$$x = 89\cdot0.$$

Granting that lactic acid is monobasic, that in the silver salt one atom of hydrogen is replaced by silver, it follows that the molecular weight of the free (lactic) acid must = 89 + 1 = 90. Consequently the simplest empiric formula of the acid, $CH_2O = 30$, must be tripled. Hence, the molecular formula of the free acid is $C_3H_6O_3 = 90$:

$C_3 = 36$		40·0
$H_6 = 6$		6·7
$O_3 = 48$		53·3
90		100·0

In studying a base, the platinum double salt is usually prepared. The constitution of these double salts is analogous to that of ammonium platinichloride $(NH_4)_2PtCl_6$—the ammonia being replaced by the base. The quantity of platinum in the double salt is determined by ignition, and calculating the quantity of the constituent combined with one atom of Pt (195·2 parts). From the number found, six atoms of chlorine and two atoms of hydrogen are subtracted, and the result is then divided by two ; the final figure will be the equivalent or molecular weight of the base.

Or, the substance is subjected to reactions of various kinds, *e.g.* the substitution of its hydrogen by chlorine. The simplest formula of acetic acid, as described above, is CH_2O. By substitution three acids can be obtained from acetic acid. These, upon treatment with nascent hydrogen, revert to the original acetic acid. They are—

$C_2H_3ClO_2$—Monochloroacetic Acid,
$C_2H_2Cl_2O_2$—Dichloroacetic Acid, and
$C_2HCl_3O_2$—Trichloroacetic Acid.

Consequently, there must be three replaceable hydrogen atoms in the acid. This would lead us to the formula $C_2H_4O_2$ for it. (Comp. also *Ladenburg* : Die Theorie der aromatischen Verbindungen (1876), p. 10.)

Knowing the molecular value of an analysed compound, it will often be necessary to multiply its *empirical* formula to obtain one which will express the number of atoms contained in the molecule. This will be the *empirical molecular formula.*

(2) *Determination of the Molecular Weight from the Vapour Density*

This method is limited to those substances which can be volatilized without undergoing decomposition. It is based upon the law of Avogadro, according to which equal volumes of all gases and vapours at like temperature and like pressure contain an equal number of molecules. The molecular weights are therefore proportional to the densities. The fundamental molecular weight is that of oxygen, which for practical reasons is given the value of 32·000. The molecular weight of hydrogen is, on this basis, 2·02 : in many cases, the density is referred to air as a basis, which is assumed to have the molecular weight 29.

The molecular weight of an unknown gas is calculated from its density

(*a*) relative to	hydrogen,	by multiplying by	2·02
(*b*) ,,	oxygen,	,, ,,	32·00
(*c*) ,,	air,	,, ,,	29·00

		Molecular Weight. (O = 16.)	Specific Gravity. (Air = 1.)
Hydrogen	H_2	= 2·02	0·0693
Oxygen	O_2	= 32·00	1·1060
Water	H_2O	= 18·02	0·622
Methane	CH_4	= 16·0	0·553

Experience has shown that the results arrived at by the chemical method and those obtained from the vapour density—are almost always identical. If a variation should occur, it is invariably in consequence of the substance undergoing decomposition, or dissociation, in its conversion into vapour.

Two essentially different methods are employed in determining the vapour density. According to one, by weighing a vessel of known capacity filled with vapour, the weight of the latter is ascertained—method of *Dumas* and of *Bunsen*; in accordance with the other, a weighed quantity of substance is vaporized and the volume of the resulting vapour determined. In the latter case the vapour volume may be directly measured—methods of *Gay-Lussac* and *A. W. Hofmann*; or it may be calculated from the equivalent quantity of a liquid expelled by the vapour—*displacement methods.* The first three methods, of which a fuller description may be found in more extended text-books, are seldom employed at present in laboratories, because the method of *V. Meyer*, which is characterized by simplicity in execution, affords sufficiently accurate results for all ordinary purposes.

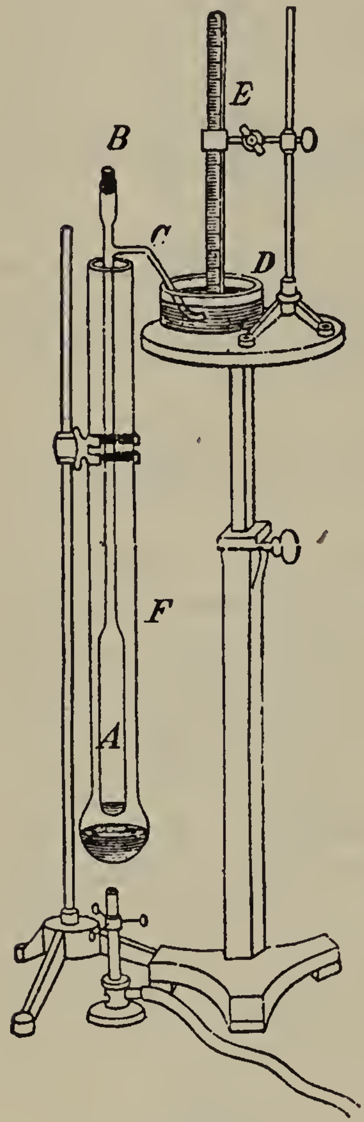

FIG. 5.

Method of Victor Meyer.— *Determination of vapour density by displacement of air* (Ber. **11**, 1867, 2253). A weighed quantity of substance is vaporized in an enclosed space, and the volume of air which it displaces is measured. Fig. 5 represents the apparatus constructed for this purpose. It consists of a narrow glass tube, ending in a cylindrical vessel, *A*. The upper, somewhat enlarged opening, *B*, is closed with an india-rubber stopper. A short capillary side tube, *C*, conducts the displaced air into the water-bath, *D*. The substance is weighed out in a small glass tube provided with a stopper, and is vaporized in *A* (improvements, see J. Ind. Eng. Chem. **4**, 684 : J.A.C.S. **39**, 2350), the escaping air being collected in the eudiometer, *E*. The vapour-bath, used in heating *A*, consists of a wide glass cylinder, *F* (Ber. **19**, 1862), whose lower, somewhat enlarged end, is closed and filled with a liquid of known boiling point. The liquid employed is determined by the substance under examination; its boiling point must be above that of the latter. Some of the liquids in use are water (100°), xylene (about 140°), aniline (184°), ethyl benzoate (213°), amyl benzoate (261°), and diphenylamine (310°).

The vapour density, S, equals the weight of the vapour, P (the same, naturally, as the weight of the substance employed), divided by the weight of an equal volume of air, P′—

$$S = \frac{P}{P'}$$

1 c.c. of air at 0° and 760 mm. pressure weighs 0·001293 gram. The air volume V_t, found at the observed temperature is under the pressure $p - s$, in which p indicates the barometric pressure and s the tension of the aqueous vapour at temperature t. The weight then would be—

$$P' = 0{\cdot}001293 \; . \; V_t . \frac{1}{1 + 0{\cdot}00367t} \; . \; \frac{p - s}{760}.$$

Consequently the vapour density sought is—*

$$S = \frac{P(1 + 0{\cdot}00367t)760}{0{\cdot}001293. \; V_t(p - s)}.$$

The displaced air may be collected in the *gas-baroscope* (compare p. 8). (Ber. **27**, 2267.)

V. Meyer's method yields results that are sufficiently accurate in practice,

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* It is simpler to make the reduction to 760 mm. 0° by comparison with a normal volume (p. 8).

because in deducing the molecular weight from the vapour density, relatively large numbers are considered and the little differences do not come into consideration. A greater inaccuracy may arise in the method of introducing the substances into the apparatus because air is apt to enter the vessel. *L. Meyer* (Ber. **13**, 991), *Piccard* (Ber. **13**, 1080), *Mahlmann* (Ber. **18**, 1624), and *V. Meyer* and *Biltz* (Ber. **21**, 688) have suggested various devices to avoid this source of error. To test the liability to decomposition of the substance at the temperature of the experiment, a small portion of it may be heated in a glass bulb drawn out to a long point (Ber. **14**, 1466).

Substances boiling above 300° are heated in a metal-bath (Ber. **11**, 2255). Porcelain vessels are used when the temperature required is so high as to melt glass, and the heating is then carried out in a Perrot's gas oven (Ber. **12**, 1112). Where air affects the substances in vapour form, the apparatus is filled with pure nitrogen (Ber. **18**, 2809 : **21**, 688). If the substances under investigation attack porcelain, tubes of platinum are substituted for the latter, which are enclosed in glazed porcelain tubes, and then heated in furnaces (Ber. **12**, 2204 : Z. physik. Chem. **1**, 146 : Ber. **21**, 688). This form of apparatus allows of the simultaneous determination of temperature (Ber. **15**, 141 : Z. physik. Chem. **1**, 153).

For modifications in displacement methods of determining the density of gases, consult *V. Meyer* (Ber. **15**, 137, 1161, 2771) ; *Langer* and *V. Meyer*, Pyrotechnische Untersuchungen, 1885 ; *Crafts* (Ber. **13**, 851 : **14**, 356 : **16**, 457). For air-baths and regulators see *L. Meyer* (Ber. **16**, 1087 : **17**, 478).

Modifications of the displacement method, adapted for work under reduced pressure, have been proposed by *La Coste* (Ber. **18**, 2122), *Schall* (Ber. **22**, 140, with bibliography : Ber. **27**, R. 604), *Eyckmann* (Ber. **22**, 2754), *V. Meyer* and *Demuth* (Ber. **23**, 311) ; *Richards* (Ber. **23**, 919, note), *Neuberg* (Ber. **24**, 729, 2543).

For further methods see *Nilson* and *Pettersson* (Ber. **17**, 987 : **19**, R. 88 : J. pr. Chem. **33**, 1) ; *Biltz* (Ber. **21**, 2767).

(3) *Determination of the Molecular Weight of Substances when in Solution*

1. **By Means of Osmotic Pressure.**—According to the theory of solutions developed by *van 't Hoff* (Z. physik. Chem. **1**, 481 : **3**, 198 : Ber. **27**, 6),* chemical substances, when in dilute solution, behave as though they were in the form of a gas or vapour ; so that the laws of *Boyle* and *Gay-Lussac*, and the hypothesis of *Avogadro*, apply also to dilute solutions. We know that the gas particles exert pressure, and it is also true that compounds, when dissolved, exert a pressure, which is directly expressed or shown by osmotic phenomena, and hence it is termed *osmotic pressure.* This pressure is equal to that which would be exerted by an equal amount of the substance, if it were converted into a gas, and occupied the same volume, at the same temperature, as the solution. Solutions containing molecular quantities of different substances exert the same osmotic pressure. It is, therefore, possible, as in the case of gas pressure, to deduce directly the molecular weight of the substance in solution from its osmotic pressure.

Pfeffer has determined osmotic pressure by means of artificial cells having semi-permeable walls. If suitably modified, this method promises to be of wide applicability (*Ladenburg*, Ber. **22**, 1225).

The *plasmolytic method* of *de Vries* for the determination of osmotic pressure, is based upon the use of living plant-cells, in place of which *Hamburger* employed red blood corpuscles (Z. physik. Chem. **2**, 415 : **14**, 424).

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* See Ostwald's Grundriss der allgemeinen Chemie, 7. Aufl. 1923 ; Lothar Meyer-Rimbach Grundzüge der theoretischen Chemie, 4. Aufl. 1907.

The molecular weight is most simply calculated by the general formula for gases: $pv = RT$, in which R represents a constant, and T the absolute temperature, calculated from − 273°. If this equation is also to include the hypothesis of *Avogadro* (that the molecular weights of gases or dissolved substances occupy the same volume at like temperature and pressure), then molecular quantities of the substances must always be taken into consideration. The constant equals 84700 for gram-molecular weights (2·02 grams hydrogen, or 32·00 grams oxygen) at the temperature 0° (or 273°), and the pressure (gas or osmotic pressure) of 76 cm. of mercury.

$$p.v = 84700 \cdot T.^{*}$$

where v represents the volume corresponding to the gram-molecular weight ($v = \frac{M}{a}$, in which a is the weight in grams of 1 c.c. of the gas, or dissolved substance, contained in 1 c.c. of the solution). After substitution the formula reads:

$$p.13 \cdot 59 \times \frac{M}{a} = 84700\ (273 + t),$$

with the four variables p, M, a and t. If three of these be given the fourth can be calculated. Consequently, the molecular weight M is found from the formula—

$$M = \frac{a.84700(273 + t)}{p \cdot 13 \cdot 59} = \frac{a.618(273 + t)}{p}.$$

2. **From the Lowering of the Vapour Pressure or the Raising of the Boiling Point.**—The lowering of the vapour pressure of solutions is closely connected with osmotic pressure. Solutions at the same temperature have a lower vapour pressure (f') than the pure solvent (f), and consequently boil at a higher temperature than the latter. The lowering in pressure ($f - f'$) is in proportion to the quantity of the substance dissolved (*Wüllner*), according to the equation $\frac{f - f'}{f} = k\,g$, in which k represents the "relative lowering of the vapour pressure" $\left(\frac{f - f'}{f}\right)$ for 1 per cent. solutions, and g their percentage content.

If the lowering be referred not to equal quantities, but to molecular quantities of the substances dissolved, it is found that equi-molecular solutions (those containing molecular quantities of the different substances in equal amounts in the same solvent) show equal lowering—the molecular vapour pressure lowering is constant:

$$M.\frac{f - f'}{f} = C.$$

Again, on comparing the relative lowering of vapour pressure in different solvents, it will be found also that they are equal, if equal amounts of the substances are dissolved in molecular quantities of the solvent. In its broadest sense the law would read: The lowering of vapour-pressure is to the vapour-pressure of the solvent (f) as the number of molecules of the dissolved body (n) is to the total number of molecules ($n + N$):

$$\frac{f - f'}{f} = \frac{n}{n + N}.$$

Substituting $\frac{g}{m}$ and $\frac{G}{M}$ (g and G represent the weight quantities of the substance and the solvent; m and M are their molecular weights), for n and N, the molecular weights, can readily be calculated.

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* $R = \frac{pv}{T}$; $p = 1033 = 76 \times 13 \cdot 59$ (sp. gr. of mercury); $v = 22400 = 32 \cdot 0$ 0·001430 (wt. of 1 c.c. of oxygen). $R = \frac{1033 \times 22400}{273}$.

F. M. Raoult (1887) discovered these relationships and put them forward as being empirical. Soon after *van 't Hoff* (Z. physik. Chem. **3**, 115) deduced them theoretically from the osmotic pressure. They are only of value for substances non-volatile as compared with the solvent, or for such as volatilize with difficulty, and show the same abnormalities as are observed with osmotic pressure and depression in the freezing point.

The methods for the determination of vapour pressure are yet too little known and primitive in their nature to be applied in the practical determination of molecular weights (Ber. **22**, 1084 : Z. physik. Chem. **4**, 538). Far more simple and exact is the determination of the rise in the boiling point, which corresponds with this (*Beckmann*, Z. physik. Chem. **4**, 539 : **6**, 437 : **8**, 223 : **15**, 656 : Ber. **27**, R. 727 : **28**, R. 432).

Method of Beckmann.—A tube, *A* (Fig. 6), is employed as the boiling vessel, and is provided with two side tubes t_1 and t_2. The substance under examination is introduced through t_1 ; a condenser, *N*, is attached to t_2, and a calcium chloride tube may be inserted at *M*. Garnets or fragments of platinum are introduced into the main tube, followed by the solvent, and finally the opening is closed by a differential thermometer (*Beckmann*, Z. physik. Chem. **51**, 329), of which the bulb must be completely covered by the liquid. The boiling tube is surrounded with an air-bath consisting of a mica cylinder, *g*, and two glass-wool plugs, h_1 and h_2. When dealing with liquids of high boiling point the air-bath may be replaced by a vapour-bath made of glass or porcelain, which is charged with the same liquid as that which is employed as the solvent ; otherwise the boiling tube may be heated directly on an asbestos netting over a micro-burner. The boiling point of the pure solvent is first read, and then again after a known quantity of the solute has been introduced down the tube *t*. A rise of temperature is observed, and should be taken after each of several successive additions of weighed quantities of the solute.

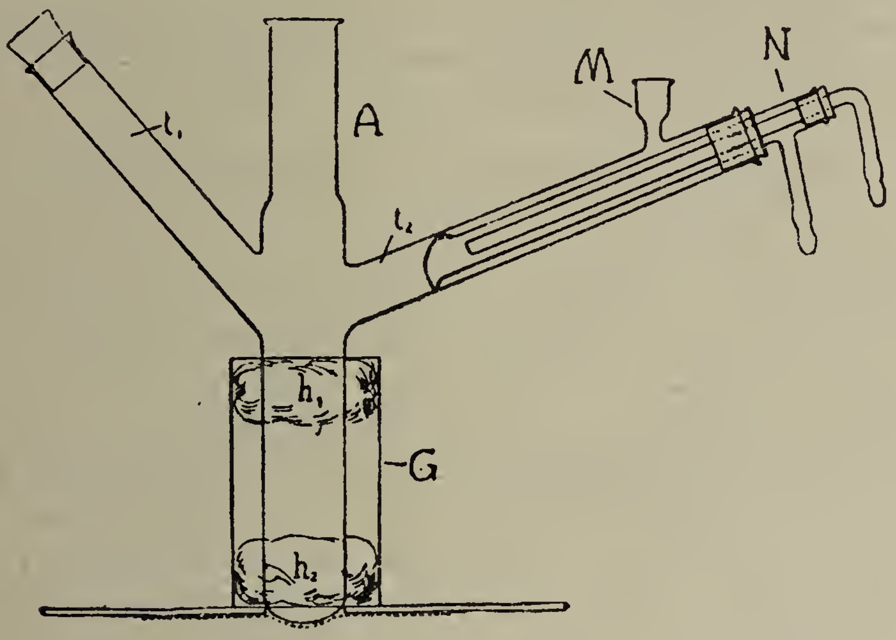

Fig 6.

A modification of the apparatus has been devised by *Beckmann* (Z. physik. Chem. **44**, 161) based on that of *Sakurai* and *Landsberger* (Ber. **31**, 458 : **36**, 1555). In this form, the temperature of the solution is raised by passing into it the vapour of the solvent, whereby continuous readings can be taken of the boiling point of the solution of a constant weight of solute in an increasing quantity of solvent. *S. Arrhenius* has deduced a formula for the molecular rise in boiling point, which is perfectly analogous to that of *van 't Hoff* for the molecular depression of the freezing point. The molecular rise is expressed by $d = 0{\cdot}02.\frac{T^2}{w}$, in which T represents the absolute boiling point, and *w* the heat of evaporation of the solvent. Upon dissolving 1 gram-molecule of a substance, *i.e.* if the molecular weight of the body is *m*, then *m* grams of it in 100 grams of solvent, the boiling point will be raised $d°$; upon dissolving p grams of the substance in 100 gr. of solvent the rise will be $d_1°$ whence $d_1 = d.\frac{P}{m}$; from which

$$m = p.\frac{d}{d_1}$$

where

p = the weight (in grams) of the substance, dissolved in 100 grams of the solvent,

d = molecular rise in boiling point $\left(= 0{\cdot}02.\frac{T^2}{w}\right)$,

d_1 = observed rise in boiling point.

The molecular rise of the boiling point in the case of ether is 21·1°, of chloroform 36·6°, and of acetic acid 25·3°. Further values, see *Landolt-Börnstein*, Physikalisch-chemische Tabellen (5. Aufl. 1923).

Micro-apparatus for molecular weight determination, see *Pregl*, Die quantitative organische Mikroanalyse, 1923.

Rieche (Ber. **59**, 2181 : *modifications*, Chem. Ztg. **1927**, 568) has devised a useful micro-apparatus, whereby with the use of 3–4 grams of solvent, a molecular weight can be determined using 15–25 mgm. of substance.

3. **From the Depression of the Freezing Point.**—The molecular weights of dissolved substances are accurately and readily deduced from the depression of the freezing points of their solutions. *Blagden* in 1788, and *Rudorff* in 1861, found that the depression of the freezing points of crystallizable solvents, or substances (as water, benzene, and glacial acetic acid), is proportional to the quantity of substance dissolved by them. The later researches of *Coppet* (1871), and especially those of *Raoult* (1882), have established the fact that when molecular quantities of different substances are dissolved in the same amount of a solvent, they show the same depression in their freezing points (*Law of Raoult*). If t represents the depression produced by p grams of a substance dissolved in 100 grams of the solvent, the coefficient of depression $\frac{t}{p}$ will be the depression for 1 gram of substance in 100 grams of the solution.* The *molecular depression* is the product obtained by multiplying the depression coefficient by the molecular weight of the dissolved substances. This is a constant for all substances having the same solvent :

$$M.\frac{t}{p} = C.$$

Raoult's experiments show the constant to have the following mean values : for benzene, 49 ; for glacial acetic acid, 39 ; for water, 19. When the constant is known, the molecular weight is calculated as follows :

$$M = C\frac{p}{t}.$$

A comparison of the constants found for different solvents will disclose the fact that they bear the same ratio to each other as the molecular weights—that consequently the quotient obtained from the molecular depressions and molecular weights is a constant value of about 0·62. It means, expressed differently, that the molecule of any one substance dissolved in 100 molecules of a liquid lowers the point of solidification very nearly 0·62°.

These empirical laws, discovered by *Coppet* and *Raoult*, have been theoretically deduced by *Guldberg* (1870) and *van 't Hoff* (1886) from the diminution of vapour

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* *Arrhenius* (Z. physik. Chem. **2**, 493) expresses the content of solutions by the weight in grams of the substances contained in 100 c.c. of the solution.

pressure and of osmotic pressure. The constant C is obtained for the various solvents, from the formula $0{\cdot}02\frac{T^2}{w}$, where T indicates the absolute temperature of solidification of the solvent, and w is its latent heat of fusion. In this way *van 't Hoff* calculated the constants for benzene (53), acetic acid (38·8), water (18·9) and camphor (400).

The laws just described can only be employed in their simple form in the case of indifferent or but slightly chemically active substances.

All electrolytes, *i.e.* salts, strong acids, and bases, behave unexpectedly in that the depressions of freezing point, the change in osmotic pressure, and the lowering of vapour pressure as found experimentally are all greater than their calculated values; the electrolytic dissociation theory of *Arrhenius* (Z. physik. Chem. **1**, 577, 631 : **2**, 491 : Ber. **27**, R. 542) accounts for this by the assumption that the electrolytes have separated into their free ions. However, even non-electrolytes frequently exhibit abnormalities, generally the opposite of the above. This seems to be due to the fact that the substances held in solution had not completely broken up into their individual molecules. The most accurate results are obtained by operating with very dilute solutions, and by employing glacial acetic acid or phenol as solvent. This dissociates solids most readily.

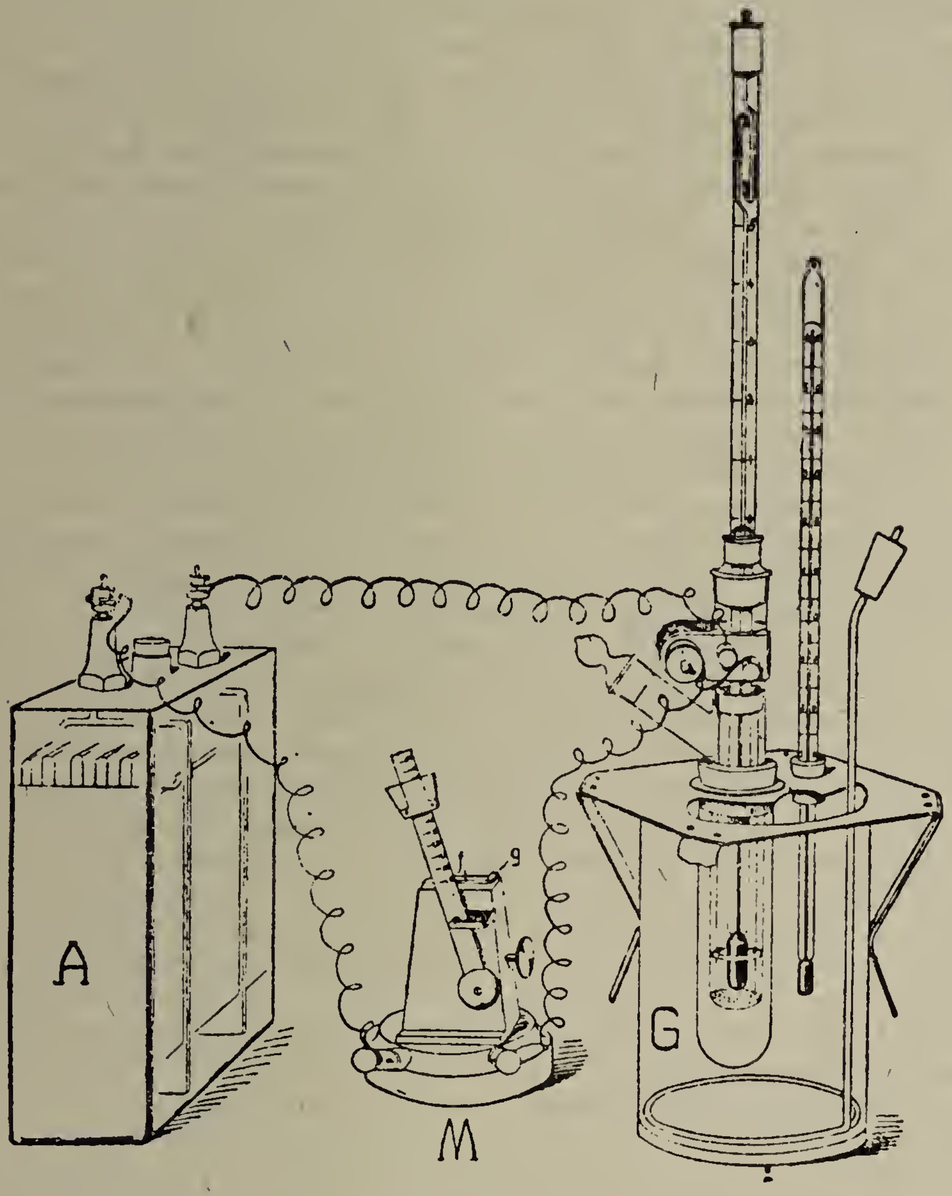


FIG. 7.

Various forms of apparatus suitable for the above purpose, and methods of working have been proposed by *Auwers* (Ber. **21**, 711), *Holleman* (Ber. **21**, 860), *Hentschel* (Z. physik. Chem. **2**, 307), *Beckmann* (Z. physik. Chem. **2**, 638), *Eykmann* (Z. physik. Chem. **2**, 964), *Klobukow* (Z. physik. Chem. **4**, 10), and *Baumann* and *Fromm* (Ber. **24**, 1431).

Method of Beckmann.—A thick-walled test tube, 2–3 cm. in diameter, to which a side tube has been fused (Fig. 7), is partially filled with 10–15 gm.

of solvent, weighed accurately. A platinum stirrer is inserted, which terminates at its upper end in a platinized or enamelled iron ring. The freezing tube is then closed with a stopper carrying a Beckmann thermometer (p. 19). Above the iron ring of the stirrer is fixed a small electromagnet, which is energized by the accumulators *A* at periods determined by the metronome *M*. The stirrer is thus kept continuously in motion, whilst the injurious effect of the atmospheric moisture is avoided. The lower part of the freezing tube is fixed by means of a cork inside a wider tube in order to prevent a too rapid fall of temperature when the apparatus is plunged into a beaker containing a freezing mixture. When the solvent chosen is acetic acid (solidifying about 16°) cold water may be employed; for benzene (solidifying about 5°), ice-water is suitable. The freezing point of the solvent is then determined, by cooling it to 1–2° below its solidifying point and then starting crystallization by stirring, or by the introduction of scraps of platinum foil or by "inoculation" with a crystal of the substance forming the solute. The thermometer then suddenly rises a little, and the freezing point is taken to be that at which the mercury remains constant for a little while. After allowing the mass to thaw, a carefully weighed quantity of the solid to be examined is introduced down the side tube, and allowed to dissolve. The freezing point of the solution is then determined in a similar manner to that just described (Ber. **28**, R. 412 : C. 1910, I. 241 : II. 361 : Z. physik. Chem. **40**, 192 : **44**, 169).

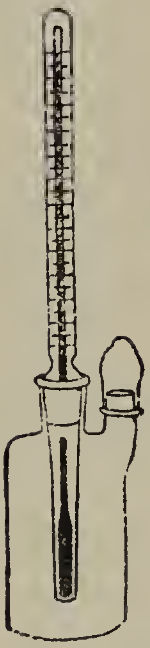


Fig. 8.

Eykmann's Method (Ann. **273**, 98) requires phenol as the solvent (melting about 38°), whereby considerable simplification is possible. Its molecular depression is greater than that of benzene, and has been calculated theoretically as being 76 (p. 17). Fig. 8 represents the form of apparatus, which consists of a flask with two tubulures, in one of which a thermometer is fixed, and over the other is placed a ground-glass cap.

The investigations of *Paterno* and others show, contrary to earlier observations, that when benzene is employed as the solvent the carbon derivatives mostly yield normal results; the exceptions being the alcohols, phenols, acids, oximes, and pyrrole (Ber. **22**, 1430 and Z. physik. Chem. **5**, 94 : Ber. **27**, R. 845 : **28**, R. 974).

Naphthalene, molecular-depression about 70, is also used as a solvent in this method (Ber. **22**, 2501 : **23**, R. 1 : **24**, 1431).

Rast (Ber. **55**, 1051, 3727) has devised a simple, well-tested micro-method for molecular weight determinations. He uses camphor as a solvent, which has the high molecular depression of C = 400 (for 100-gm. solvent). On account of the high solubility of many organic compounds in camphor it is possible to carry out the determination in a melting-point flask with an ordinary thermometer graduated in degrees. A few milligrammes of substance suffice for a determination.

Consult Ber. **28**, 804 for a method of determining molecular weights from the *decrease in solubility*.

For the determination of molecular weight from *molecular solution-volume*, see Ber. **29**, 1023.

THE CHEMICAL CONSTITUTION OF THE CARBON COMPOUNDS

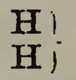
Early Theories.—The opinion that the cause of chemical affinity resided in electrical forces was first expressed in the commencement of the last century, when the remarkable decompositions of chemical bodies through the agency of the electric current were discovered. It was assumed that the elementary atoms possessed different electrical polarities, and that the elements were arranged in a series according to their electrical behaviour. Chemical union depended on the equalization of different electricities. The *dualistic* idea of the constitution of compounds was a necessary consequence of this hypothesis. According to it, every chemical compound was composed of two groups, electrically different, and these were further made up of two different groups or elements. Thus, salts were viewed as combinations of electro-positive bases (metallic oxides), with electro-negative acids (acid anhydrides), and these, in turn, were held to be binary compounds of oxygen with metals and non-metals. With this as basis there was constructed the *electro-chemical, dualistic theory of Berzelius*, which almost exclusively dominated chemical science in Germany until the beginning of 1860.

The principles predominating in inorganic chemistry were also applied to organic substances. It was thought that in the latter complex groups (radicals) played the same *rôle* as that of the elements in inorganic chemistry. Organic chemistry was defined as the *chemistry of the compound radicals* (*Liebig*, 1832), and led to the *chemical-radical theory*, which flourished in Germany simultaneously with the *electro-chemical theory*. According to this view, the object of organic chemistry was the investigation and isolation of radicals, in the sense of the dualistic idea, as the more intimate components of the organic compounds, and by this means they sought to explain the constitution of the latter. (*Liebig* and *Wöhler*, Ueber das Radical der Benzoësäure, Ann. **3**, 249; *Bunsen*, Ueber die Kakodylverbindungen, Ann. **31**, 175: **37**, 1: **42**, 14: **46**, 1.)

In the meantime, about 1830, France contributed facts not in harmony with the electro-chemical, dualistic theory. It had been found that the hydrogen in organic compounds could be replaced (substituted) by chlorine and bromine, without any important change in the character of the compounds. To the electro-negative halogens was ascribed a chemical function similar to electro-positive hydrogen. This showed the electro-chemical hypothesis to be erroneous. The dualistic idea was superseded by a *unitary* theory. Laying aside all the primitive speculations on the nature of chemical affinity, the chemical compounds began to be looked upon as being constituted in accordance with definite fundamental forms—*types*—in which the individual elements could be replaced by others (early *type theory* of *Dumas*, *nucleus theory* of *Laurent*). Dumas, however, distinguished between *chemical* types and *mechanical* types. He considered substances to have the same *chemical* type, to be of the same species, when they possessed the same fundamental properties, *e.g.* acetic and chloracetic acids. Like *Regnault*, he considered that they were of the same *mechanical* type, belonged to the same natural family, when they were related in structure but showed a different chemical character, *e.g.* alcohol and acetic acid. At the same time, the dualistic view on the pre-existence of radicals was refuted.

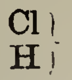
The correct establishment of the ideas of *equivalent*, *atom*, and *molecule* (*Laurent* and *Gerhardt*) was an important consequence of the typical unitary idea of chemical compounds. By means of it a correct foundation was laid for further generalization. The molecule having been accepted as a chemical unit, the study of the grouping of atoms in the molecule became possible, and chemical constitution could again be more closely examined. The investigation of the reactions of double decomposition, whereby single atomic groups (radicals or residues) were preserved and could be exchanged (*Gerhardt*); the important discoveries of the amines or substituted ammonias by *Würtz* (1849) and *Hofmann* (1849); the epoch-making researches of *Williamson* and *Chancel* (1850), upon the composition of ethers; and the discovery of acid-forming oxides by *Gerhardt* (1851),—led to a "type" explanation of the individual classes of compounds. *Williamson* referred the alcohols and ethers to the water type. *A. W. Hofmann* deduced the substituted ammonias from ammonia. The "type" idea found its culmination in the *type theory of Gerhardt* (1853), which was nothing more than an amalgamation of the early type or substitution theory of Dumas and Laurent with the radical theory of Berzelius and Liebig. The molecule was its basis, in which a further grouping of atoms was assumed. The conception of radicals became different; they were no longer regarded as atomic groups that could be isolated and compared with elements, but as molecular residues which remained unaltered in certain reactions.

Comparing the carbon compounds with the simplest inorganic derivatives, Gerhardt referred them to the following principal fundamental *forms* or *types*:



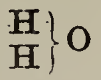
$$\left.\begin{matrix}H\\H\end{matrix}\right\}$$

Hydrogen.



$$\left.\begin{matrix}Cl\\H\end{matrix}\right\}$$

Hydrogen chloride.



$$\left.\begin{matrix}H\\H\end{matrix}\right\}O$$

Water.

$$\left.\begin{matrix}H\\H\\H\end{matrix}\right\}N$$

Ammonia.

From these they could be obtained by substituting the compound radicals for hydrogen atoms. All compounds that could be viewed as consisting of two directly combined groups were referred to the hydrogen and hydrogen chloride types, *e.g.*:

$$\underset{\text{Ethyl hydride.}}{\left.\begin{matrix}\mathrm{C_2H_5}\\ \mathrm{H}\end{matrix}\right\}}\qquad \underset{\text{Ethyl chloride.}}{\left.\begin{matrix}\mathrm{C_2H_5}\\ \mathrm{Cl}\end{matrix}\right\}}\qquad \underset{\text{Cyanogen hydride.}}{\left.\begin{matrix}\mathrm{CN}\\ \mathrm{H}\end{matrix}\right\}}\qquad \underset{\text{Ethyl cyanide.}}{\left.\begin{matrix}\mathrm{C_2H_5}\\ \mathrm{CN}\end{matrix}\right\}}\qquad \underset{\text{Acetyl chloride.}}{\left.\begin{matrix}\mathrm{C_2H_3O}\\ \mathrm{Cl}\end{matrix}\right\}}$$

It was customary to refer all those bodies derivable from water by the replacement of hydrogen, to the water type:

$$\underset{\text{Alcohol.}}{\left.\begin{matrix}\mathrm{C_2H_5}\\ \mathrm{H}\end{matrix}\right\}\mathrm{O}}\qquad \underset{\text{Acetic acid.}}{\left.\begin{matrix}\mathrm{C_2H_3O}\\ \mathrm{H}\end{matrix}\right\}\mathrm{O}}\qquad \underset{\text{Ethyl ether.}}{\left.\begin{matrix}\mathrm{C_2H_5}\\ \mathrm{C_2H_5}\end{matrix}\right\}\mathrm{O}}\qquad \underset{\text{Acetic anhydride.}}{\left.\begin{matrix}\mathrm{C_2H_3O}\\ \mathrm{C_2H_3O}\end{matrix}\right\}\mathrm{O}}$$

Associated types were included with the principal types. Thus, with the fundamental type $\left.\begin{matrix}\mathrm{Cl}\\ \mathrm{H}\end{matrix}\right\}$ were arranged, as subordinates, the types $\left.\begin{matrix}\mathrm{Br}\\ \mathrm{H}\end{matrix}\right\}$ $\left.\begin{matrix}\mathrm{I}\\ \mathrm{H}\end{matrix}\right\}$; with the water type $\left.\begin{matrix}\mathrm{H}\\ \mathrm{H}\end{matrix}\right\}\mathrm{O}$ that of $\left.\begin{matrix}\mathrm{H}\\ \mathrm{H}\end{matrix}\right\}\mathrm{S}$, etc.

All derivatives of ammonia were referred to the ammonia type:

$$\underset{\text{Methylamine.}}{\left.\begin{matrix}\mathrm{CH_3}\\ \mathrm{H}\\ \mathrm{H}\end{matrix}\right\}\mathrm{N}}\qquad \underset{\text{Trimethylamine.}}{\left.\begin{matrix}\mathrm{CH_3}\\ \mathrm{CH_3}\\ \mathrm{CH_3}\end{matrix}\right\}\mathrm{N}}\qquad \underset{\text{Acetamide.}}{\left.\begin{matrix}\mathrm{C_2H_3O}\\ \mathrm{H}\\ \mathrm{H}\end{matrix}\right\}\mathrm{N}}\qquad \underset{\text{Cyanic acid.}}{\left.\begin{matrix}\mathrm{CO}\\ \mathrm{H}\end{matrix}\right\}\mathrm{N}}$$

The types of Gerhardt were chemical types, as he himself expresses it: "Mes types sont des types de double décomposition." It is thus understood that he included the type $\left.\begin{matrix}\mathrm{Cl}\\ \mathrm{H}\end{matrix}\right\}$ with that of $\left.\begin{matrix}\mathrm{H}\\ \mathrm{H}\end{matrix}\right\}$.

These types no longer possessed their early restricted meaning. Sometimes a compound was referred to different types, according to the transpositions the formula was intended to express. Thus aldehyde was referred to the hydrogen or water type; cyanic acid to the water or ammonia type:

$$\left.\begin{matrix}\mathrm{C_2H_3O}\\ \mathrm{H}\end{matrix}\right\}\quad\text{and}\quad \left.\begin{matrix}\mathrm{C_2H_3}\\ \mathrm{H}\end{matrix}\right\}\mathrm{O},\qquad \left.\begin{matrix}\mathrm{CN}\\ \mathrm{H}\end{matrix}\right\}\mathrm{O}\quad\text{and}\quad \left.\begin{matrix}\mathrm{CO}\\ \mathrm{H}\end{matrix}\right\}\mathrm{N}$$

The development of the idea of polyatomic radicals, the knowledge that the hydrogen of carbon radicals could be replaced by the groups OH and NH_2, etc., contributed to the further establishment of *multiple* and *mixed types* (*Williamson, Odling, Kekulé*):

Compound Types:

$$\left.\begin{matrix}\mathrm{ClH}\\ \mathrm{ClH}\end{matrix}\right\}\qquad \left.\begin{matrix}\mathrm{H_2}\\ \mathrm{H_2}\end{matrix}\right\}\mathrm{O_2}\qquad \left.\begin{matrix}\mathrm{H_2}\\ \mathrm{H_2}\\ \mathrm{H_2}\end{matrix}\right\}\mathrm{N_2}$$

e.g.:

$$\underset{\text{Ethylene chloride.}}{\left.\begin{matrix}\mathrm{Cl}\\ \mathrm{C_2H_4''}\\ \mathrm{Cl}\end{matrix}\right\}}\qquad \underset{\text{Ethylene glycol.}}{\begin{matrix}\left.\begin{matrix}\mathrm{H}\\ \mathrm{C_2H_4''}\end{matrix}\right\}\mathrm{O}\\ \left.\mathrm{H}\right\}\mathrm{O}\end{matrix}}\qquad \underset{\text{Carbamide.}}{\begin{matrix}\left.\begin{matrix}\mathrm{H_2}\\ \mathrm{CO''}\end{matrix}\right\}\mathrm{N}\\ \left.\mathrm{H_2}\right\}\mathrm{N}\end{matrix}}$$

Mixed Types:

$$\left\{\begin{matrix}\left.\begin{matrix}\mathrm{Cl}\\ \mathrm{H}\end{matrix}\right\}\\ \left.\begin{matrix}\mathrm{H_2}\\ \mathrm{H_2}\end{matrix}\right\}\mathrm{O_2}\end{matrix}\right.\qquad\qquad \left\{\begin{matrix}\left.\begin{matrix}\mathrm{H}\\ \mathrm{H}\\ \mathrm{H}\end{matrix}\right\}\mathrm{N}\\ \left.\begin{matrix}\mathrm{H}\\ \mathrm{H}\end{matrix}\right\}\mathrm{O}\end{matrix}\right.$$

$$\underset{\text{Chlorhydrin.}}{\begin{matrix}\left.\begin{matrix}\mathrm{Cl}\\ \mathrm{C_3H_5'''}\end{matrix}\right\}\\ \left.\mathrm{H_2}\right\}\mathrm{O_2}\end{matrix}}\qquad \underset{\text{Oxamic acid.}}{\begin{matrix}\left.\begin{matrix}\mathrm{H_2}\\ \mathrm{C_2O_2''}\end{matrix}\right\}\mathrm{N}\\ \left.\mathrm{H}\right\}\mathrm{O}\end{matrix}}\qquad \underset{\text{Amidoacetic acid.}}{\begin{matrix}\left.\begin{matrix}\mathrm{H_2}\\ \mathrm{C_2H_2O''}\end{matrix}\right\}\mathrm{N}\\ \left.\mathrm{H}\right\}\mathrm{O}\end{matrix}}$$

The presentation of these multiple and mixed types depended on the polyatomic radicals of two or more " type-molecules," if one may so name them, becoming united into one whole—a molecule. Upon comparing these typical with the structural formulæ employed at present, we observe that the first constitute the transitional state from the empirical, unitary formulæ to those of the present day. The latter aim to express the kind of grouping of the atoms in the molecule.

The next step was the expansion of the Gerhardt type to the—

Marsh-gas type $\left.\begin{matrix}H\\H\\H\\H\end{matrix}\right\}C$ by Kekulé, 1856 (Ann. **101**, 204).

A year later Kekulé (1857) in a communication, " Ueber die sog. gepaarten Verbindungen und die Theorie der mehratomigen Radicale " (Ann. **104**, 129), indicated the idea of types by the assumption of a peculiar function of the atoms —their atomicity or basicity (valence). This he supposed to be the cause of the types of Gerhardt.

As early as 1852 Frankland had enunciated similar views in regard to the elements of the nitrogen group (Ann. **85**, 329 : **101**, 257 : *Frankland*, Experimental Researches in Pure, Applied, and Physical Chemistry, London, 1871, p. 147). Kolbe concurred with these ideas (compare his derivation of the organic compounds from the radical carbonyl C_2 and carbon dioxide C_2C_4—*Kolbe's* Lehrbuch der organischen Chemie, 1858, Bd. I. p. 567). The reason that they did not exert greater influence upon the development of theoretical chemistry is mainly due to the fact that the notions of the relations of equivalent weight and atomic weight were not clearly defined by either of these two investigators.

In his assumptions Kekulé rather returned to Dumas' mechanical types than to the double decomposition types of Gerhardt. The distinction between the type $\left.\begin{matrix}H\\H\end{matrix}\right\}$ and $\left.\begin{matrix}Cl\\H\end{matrix}\right\}$ as drawn by Gerhardt did not exist for Kekulé. The latter, in 1858, said, " It is necessary in explaining the properties of chemical compounds to go back to the elements which compose these compounds." He continues: " I do not regard it as the chief aim of our time to detect atomic groups which, owing to certain properties, may be considered radicals and thus to include the compounds under certain types, which in this way have scarcely any other significance than that of type or example formula. I am rather of the opinion that the generalization should be extended to the constitution of the radicals themselves, to the determination of the relation of the elements among themselves, and thus to deduce from the nature of the elements both the nature of the radicals and that of their compounds " (Ann. **106**, 136).

The recognition of the quadrivalence of the carbon atoms and the power they possessed of combining with each other, accounted for the existence and the combining value of radicals ; also, for their constitution (*Kekulé, l.c.*, and *Couper*, Ann. chim. phys. [3] **53**, 469). The type theory, consequently, is not, as sometimes declared, laid aside as erroneous ; it has only found generalization and amplification in a broader principle—the extension of the valence theory of Kekulé and Couper to the derivatives of carbon.

Whilst formerly it was the custom to consider in addition to *empirical* formulæ, representing merely an atomic composition of the molecule, also *rational* formulæ (Berzelius), which in reality were nothing more than reaction formulæ adopted to explain to a certain degree the chemical behaviour of a compound, Kekulé now spoke of the *manner of the union of the atoms in the molecule*, by knowledge of which the constitution of the carbon compounds may be determined (*constitutional formulæ*). Lothar Meyer next introduced the phrase " *linking of the carbon atoms*." The expression *structure* (*structural formulæ*) originated with Butlerow.

An application of the valency theory, which has been remarkably fruitful, is the *Kekulé benzene theory*. Here for the first time there was assumed to be present in a carbon compound a closed carbon-chain, a ring consisting of six carbon atoms. The rather singular stability of the aromatic bodies is due to the presence of this " benzene ring." Kórner applied these views to pyridine and deduced the pyridine ring ; and in recent years numerous other ring-systems have been suggested and substantiated.

CHEMICAL STRUCTURE OF CARBON COMPOUNDS

THEORY OF ATOMIC LINKING, OR THE STRUCTURAL THEORY

Constitutional or structural formulæ are based upon the following principles, which have been deduced from experiment and repeatedly confirmed :

1. *The carbon atom is quadrivalent.* The position of carbon in the periodic system gives expression to this fact. One carbon atom can combine at the most with four similar or dissimilar univalent atoms or atomic groups :

CH_4	CF_4	CCl_4
Methane.	Carbon tetrafluoride.	Carbon tetrachloride.

CH_3Cl	CH_3NH_2	CH_2Cl_2	$CHCl_3$
Methyl chloride.	Methylamine.	Dichloromethane.	Chloroform.

In a few compounds, such as carbon monoxide CO, the isonitriles or carbylamines $R'-N=C$ (Ann. **270**, 267) ; and fulminic acid $HO-N=C$ (Ann. **280**, 303) carbon behaves as a bivalent element : compounds are known such as the triarylmethyls, $Ar_3C\cdot$ (see Vol. II), in which carbon appears as a trivalent element.

2. *The four units of affinity of carbon are equal, i.e.* no differences can be discovered in them when they form compounds. If one of the four hydrogen atoms in the simplest hydrocarbon, CH_4, be replaced by a univalent atom or univalent atomic group, each mono-substitution product will appear in but one modification. The four hydrogen atoms are similarly combined, consequently it is immaterial which of them is replaced.

CH_3Cl	CH_3OH	CH_3NH_2
Chloromethane.	Methyl alcohol.	Methylamine.

are known in but one modification each.

The equivalence of the four valencies of carbon does not imply that the affinity of the carbon atom is divided into four independent, completely equivalent forces. The view of Claus (Ber. **14**, 432) seems more accurately to represent the facts. He assumed that the affinity with which an atom or group is attached to the carbon is primarily determined by the atoms or groups already attached to the carbon atom. The affinity available for the attachment of the hydrogen atoms in the compounds CH_3X, CH_2X_2 and CHX_3 is not equal in the three substances, but is dependent upon the larger or smaller affinities of the atom or radical X (*cf. Werner*, Ber. **39**, 1278 : *Tschitschibabin*, J. pr. Chem. [2], **86**, 381 : also Vol. II under hexaphenylethane).

3. *The carbon atoms can unite with each other.* When two carbon atoms combine the union can occur in three ways :

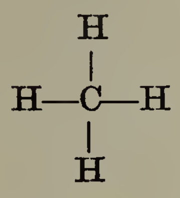
(*a*) The two carbon atoms unite with a single valence each, leaving the atomic group, $\equiv C-C\equiv$, with six free valences.

(*b*) The two carbon atoms unite with two valences each, constituting an atomic group, $=C=C=$, with four free valences.

(*c*) Two carbon atoms are united by three valences. The residual group $-C\equiv C-$ has but two uncombined valences.

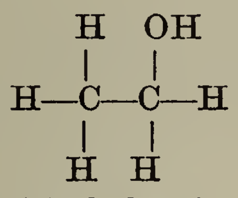
In the first case the union of the two carbon atoms is by a *single* *bond*, in the second case by a *double*, and in the third case by a *triple bond.* Carbon atoms can combine with themselves to a greater degree than the atoms of any other elements. This gives rise to carbon nuclei, and carbon skeletons, which can form either *open chains* or *closed chains* (*rings*). The uncombined valences of the carbon nuclei can saturate or take up atoms of other elements or other atomic groups. This explains the existence of the innumerable carbon compounds.

This mutual union is indicated, according to the recommendation of Couper, by lines. These formulæ represent the internal construction of the compounds, and are known as *structural formulæ* :



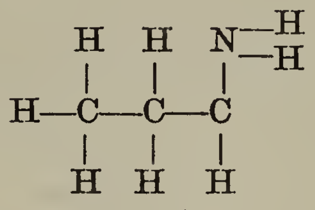
$$\begin{array}{ccccc} & & H & & \\ & & | & & \\ H & - & C & - & H \\ & & | & & \\ & & H & & \end{array}$$

Methane.



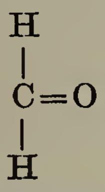
$$\begin{array}{ccccccc} & & H & & OH & & \\ & & | & & | & & \\ H & - & C & - & C & - & H \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

Ethyl alcohol.



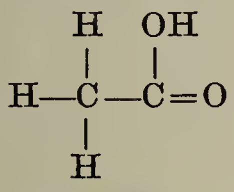
$$\begin{array}{ccccccc} & & H & & H & & N\begin{array}{l}-H\\-H\end{array} \\ & & | & & | & & | \\ H & - & C & - & C & - & C \\ & & | & & | & & | \\ & & H & & H & & H \end{array}$$

Propylamine.



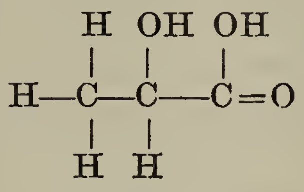
$$\begin{array}{c} H \\ | \\ C=O \\ | \\ H \end{array}$$

Formaldehyde.



$$\begin{array}{ccccc} & & H & & OH \\ & & | & & | \\ H & - & C & - & C=O \\ & & | & & \\ & & H & & \end{array}$$

Acetic acid.



$$\begin{array}{ccccccc} & & H & & OH & & OH \\ & & | & & | & & | \\ H & - & C & - & C & - & C=O \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

Lactic acid.

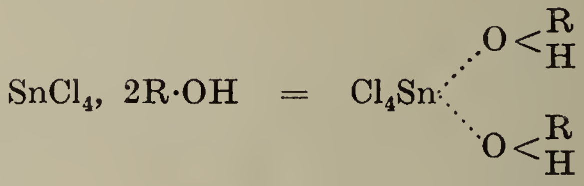
Such structural formulæ have been deduced, by the help of the valency theory, from reactions which result in the building up and the breaking down of carbon compounds. They express clearly the relations between the bonds, which, in the main, determine the behaviour of the substance. Those atoms within the molecule which are bound most directly to each other exercise the greatest influence on one another. But it must not be supposed that atoms, unconnected directly by bonds, exert no mutual influence ; such structural formulæ give no information of their relative distances apart in space. In the study of reactions where halogen atoms are substituted for hydrogen in the molecule, it is immediately apparent that such replacement takes place with varying facility. This is specially obvious in the case of the aromatic substances (see Volume II). Further, the carboxyl group reacts with different degrees of acidity varying with the individual acid. Reactions, in which the loss of some atoms causes a single bond to become a multiple one, or the formation of a ring complex, and where intra-molecular atomic migration (see p. 46) takes place, obviously depend on the mutual influence of atoms unconnected directly by bonds, as shown in the structural formulæ.

Kekulé's valency theory explains clearly the function of the main bonds in our structural formulæ, but does not deal with the subsidiary action of the various atoms on one another in the molecule. And yet one cannot go so far as to say that in each atomic constellation which constitutes a molecule, every atom exerts a chemical influence on every other. But so much can be asserted, that each atom contained in the molecule of a chemical compound is bound to each other atom in that molecule. To illustrate such attractions diagrammatically, it would be necessary to draw a network of interatomic bonds in every atomic formula. The greater or lesser strength of the bond could be indicated by a thicker or finer line. If such a diagram were examined at a certain distance, only the thick lines—Bonds of the First Order—would be seen clearly, *i.e.* practically the same in appearance as the structural formula ordinarily represented.

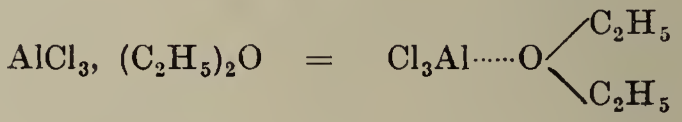
In many cases it can be deduced from the behaviour of the substance that the Bonds of the Second Order exert an influence of appreciable strength. These bonds may be described as "*Intramolecular subsidiary bonds.*"

An external sign of the presence of such subsidiary valency bonds is found in the absence of such chemical reactions as might be expected to take place by analogy with others. Another exists in the relative ease with which a group of atoms can be split off, which indicates the pre-existence in the original molecule of such a group held together by these second-order bonds (*cf. Anschütz*, Ann. **346**, 375). In other cases the failure of a reaction to take place, which might have been anticipated on the ground of analogy, is ascribed to steric hindrance, which implies that the substituent groups by their position hinder the access of the reacting substances (*C. A. Bischoff*, Ber. **23**, 620 : *V. Meyer*).

Extramolecular subsidiary valencies, Compounds of higher order,* Molecular compounds.†—Kekulé frequently expressed the view that, having regard to the constant valency of the elements, many compounds had to be described as molecular compounds. In his Rectorial address in 1877 he described the complex compounds formed by molecular attraction as molecules of higher order. The constitution of many organic compounds cannot indeed be satisfactorily represented by the simple use of the four principal carbon valencies, and according to A. Werner, these "molecular" compounds are to be regarded as held together by subsidiary valencies emanating from certain atoms. The theory of organic molecular compounds is the logical transference from inorganic chemistry of the views of Werner on the constitution of complex compounds. From the Werner-Pfeiffer standpoint, the numerous well-characterized addition products of acids and salts with alcohols, aldehydes, ketones, etc., are represented by the attachment of the organic component to the metallic atom by subsidiary links, *e.g.* :

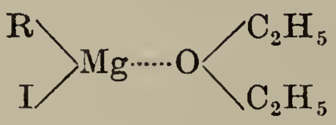


$$SnCl_4,\ 2R{\cdot}OH = Cl_4Sn\begin{matrix}\cdot\cdot O<{}^{R}_{H}\\ \cdot\cdot O<{}^{R}_{H}\end{matrix}$$

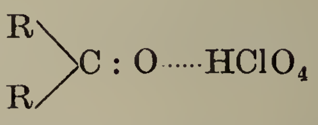


$$AlCl_3,\ (C_2H_5)_2O = Cl_3Al\cdots O<{}^{C_2H_5}_{C_2H_5}$$

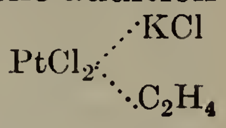
Similarly :



$$\begin{matrix}R\\I\end{matrix}>Mg\cdots O<\begin{matrix}C_2H_5\\C_2H_5\end{matrix}$$



$$\begin{matrix}R\\R\end{matrix}>C:O\cdots HClO_4$$

In so far as compounds of metallic salts with oxygen containing organic compounds are being dealt with, the subsidiary valency can be represented as between the metallic atom and the oxygen atom. In many cases, however, the precise origin of a subsidiary valency cannot be stated with certainty, and the phenomenon is regarded as the mutual saturation of two unsaturated affinity-fields. The addition products between salts and unsaturated hydrocarbons  $PtCl_2\begin{matrix}\cdot\cdot KCl\\ \cdot\cdot C_2H_4\end{matrix}$

---

* *A. Kekulé*, Die wissenschaftlichen Ziele und Leistungen der Chemie, 18 October 1877, p. 23.

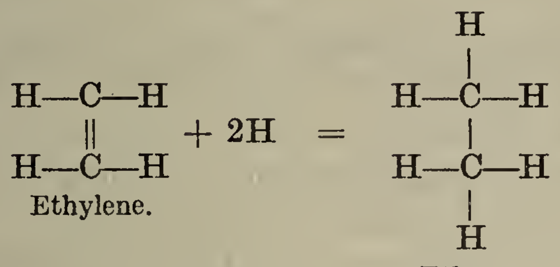
† *P. Pfeiffer*, Organische Molekülverbindungen, Stuttgart, 1927, Enke : Lecture, Z. angew. Chem. 1921, **34**, 350.

and the addition compounds between polynitro compounds and hydrocarbons or amines fall into this class, *e.g.*

$$C_6H_3(NO_2)_3,C_6H_5(CH_3) \quad \text{and} \quad C_6H_3(NO_2)_3,C_6H_5NH_2$$

The formation of molecular compounds is frequently associated with the development of colour, or of deepening of colour (*cf.* Halochromy, p. 53).

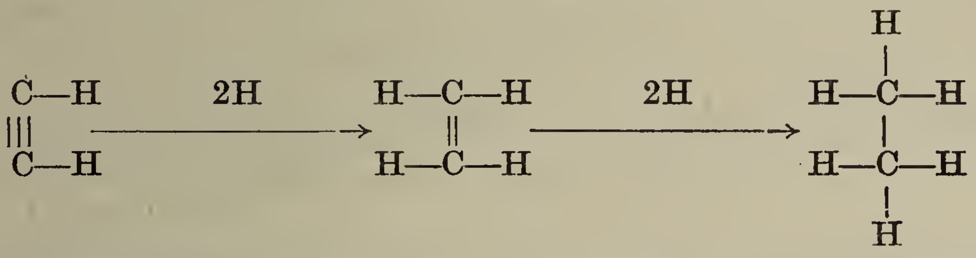
Saturated and Unsaturated Compounds.—*Saturated* carbon compounds are those in which only singly bound carbon atoms occur. No more valencies are available unless the carbon chain is broken up. *Unsaturated* compounds are those in which doubly or triply bound carbon atoms exist. As a single bond is sufficient to link carbon atoms together, a pair of carbon atoms with double bond can take up two additional valence units, if one of the double bonds becomes broken, the other remaining intact to avoid destruction of the chain, *e.g.*:



$$\begin{array}{c}H-C-H\\ \|\\ H-C-H\end{array} + 2H = \begin{array}{c}H\\ |\\ H-C-H\\ |\\ H-C-H\\ |\\ H\end{array}$$

Ethylene. Ethane.

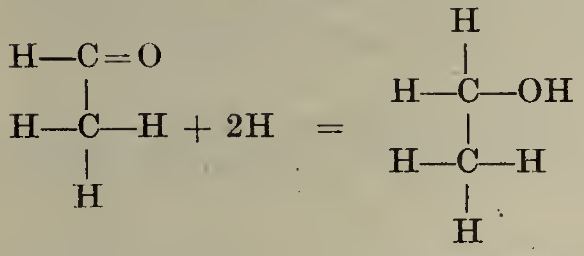
Two carbon atoms, trebly linked, can take up four valences. The dissolution of the triple union may proceed step by step, whereby it may first be changed to a double linkage and then to a single bond:



$$\begin{array}{c}C-H\\ |||\\ C-H\end{array} \xrightarrow{2H} \begin{array}{c}H-C-H\\ \|\\ H-C-H\end{array} \xrightarrow{2H} \begin{array}{c}H\\ |\\ H-C-H\\ |\\ H-C-H\\ |\\ H\end{array}$$

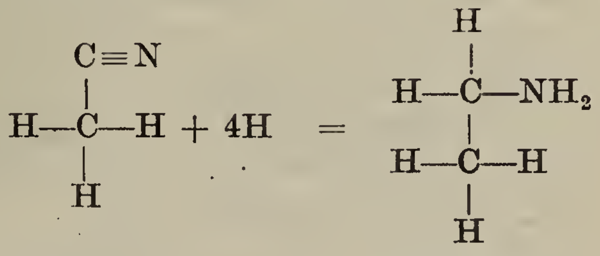
The unsaturated compounds, by the breaking down of their double and triple bonds and the addition of two or four univalent atoms, pass into saturated compounds.

This same behaviour is observed with many other compounds containing carbon and oxygen, doubly combined, $=C=O$ (aldehydes and ketones) or double and triple union of carbon and nitrogen, $=C=N-$ or $-C\equiv N$ (acid nitriles, imides, oximes). They are in the same sense unsaturated; by the breaking down of their double or triple union they change to saturated compounds in which the polyvalent atoms are linked by a single bond to each other:



$$\begin{array}{c}H-C=O\\ |\\ H-C-H\\ |\\ H\end{array} + 2H = \begin{array}{c}H\\ |\\ H-C-OH\\ |\\ H-C-H\\ |\\ H\end{array}$$

Acetaldehyde. Ethyl alcohol.

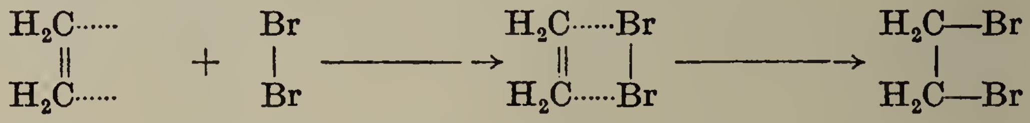


$$\begin{array}{c}C\equiv N\\ |\\ H-C-H\\ |\\ H\end{array} + 4H = \begin{array}{c}H\\ |\\ H-C-NH_2\\ |\\ H-C-H\\ |\\ H\end{array}$$

Acetonitrile. Ethylamine.

The above method of formulation of unsaturated compounds does not, without further explanation, demonstrate their most important property, their unsaturation and their ability to form addition compounds.

Thiele has attempted (Ann. **306,** 87 : **319,** 132) to overcome the difficulty of representation of unsaturated compounds by the assumption that in them the carbon atoms are actually joined by two or three valencies, but that the available affinity is not fully used up, and that there therefore remains the excess of affinity, the so-called "*partial valency,*" on each carbon atom. These partial valencies are responsible for the unsaturated nature of the compounds, and permit of addition reactions, the addendum being initially attached by means of the partial valency, and then, by rupture of the double bond, the ordinary addition product being formed, *e.g.* :



Substances containing adjacent double bonds, such as butadiene $CH_2 : CH{\cdot}CH : CH_2$, frequently form addition compounds in an unusual way, the addenda being attached to the two terminal groups instead of at one double bond, the product being $CH_2X{\cdot}CH : CH{\cdot}CH_2X$. Such a system of double bonds is referred to as a "*conjugated system,*" and the mechanism is explained by Thiele as follows. The two partial valencies on the middle carbon atoms of the system neutralize each other, those on the terminal atoms, where addition takes place, remaining free :

Examples of addition to a conjugated system are :

$$CH_2 : CH{\cdot}CH : CH_2 + 2Br \longrightarrow CH_2Br{\cdot}CH : CH{\cdot}CH_2Br$$

(Chief product.)

$$CO_2H{\cdot}CH : CH{\cdot}CH : CH{\cdot}CO_2H + 2H \longrightarrow CO_2H{\cdot}CH_2{\cdot}CH : CH{\cdot}CH_2{\cdot}CO_2H$$

Muconic acid. Dihydromuconic acid.

(*Cf.* also *Baeyer*, Ann. **251,** 271 (Dihydroterephthalic acid).)

Although many experimental facts cannot at present be brought into line with this conception, and the problem of the unsaturated compounds is by no means entirely solved by Thiele's theory of partial valencies, the idea has been of great assistance in the understanding of the behaviour of aromatic nuclei, especially of the benzene derivatives (*cf.* further, *Hinrichson*, Z. physik. Chem. **31,** 304 : Ann. **386,** 168 : Chem. Ztg. **33,** 1097 : *Strauss*, Ber. **42,** 2866 : *Borsche*, Ann. **375,** 147 : *Tschitschibabin*, J. pr. Chem. [2], **86,** 381 : Comprehensive references, see *Henrich*, Theorien der organischen Chemie, 5. Aufl. 1924, Vieweg).

A further type of unsaturated compound must be referred to in which a single carbon atom is regarded as being di- or trivalent (Ann. **298,** 202). Examples are :

$=C=O$	$=C=N{\cdot}C_2H_5$	$C=N=OH$	$(C_6H_5)_3\equiv C-$
Carbon monoxide.	Ethyl *iso*cyanide.	Fulminic acid.	Triphenylmethyl.

ELECTRONIC THEORY OF VALENCY

See *Sidgwick*, Electronic Theory of Valency, Oxford, 1927.

The modern ideas on valency really date from the independent publications of Kossel (Ann. der Phys. **49**, 229) and G. N. Lewis (J.A.C.S. **38**, 762) in 1917.

They are based upon the conception of the atom as composed of a nucleus, positively charged, surrounded by a swarm of electrons negatively charged. The nucleus is composed of a number of protons (units of positive electricity) together with a less number of electrons in close association with them. The requisite number of electrons to ensure electrical neutrality surround this nucleus. Thus carbon possesses a nucleus consisting of twelve protons and six electrons, and there are six electrons moving in orbits round the nucleus. For simplicity, these electrons may be regarded as moving in one or more concentric spheres or shells round the nucleus. It is found that if a shell contains two or eight electrons (for the simpler elements) it is stable or complete, but if an atom contains a different number it attempts to complete its outer shell, either by taking up electrons from other atoms or by giving up to other atoms the electrons it possesses in excess of the ideal number. These additional electrons are known as valency electrons and are comparatively easily removed. In the case of carbon already referred to the six external electrons are arranged as a " complete " shell of two electrons and four valency electrons (see diagram). The inert gases, helium, neon, argon, etc., possess no valency electrons : their electrons are all in complete shells and the elements are therefore chemically inert.

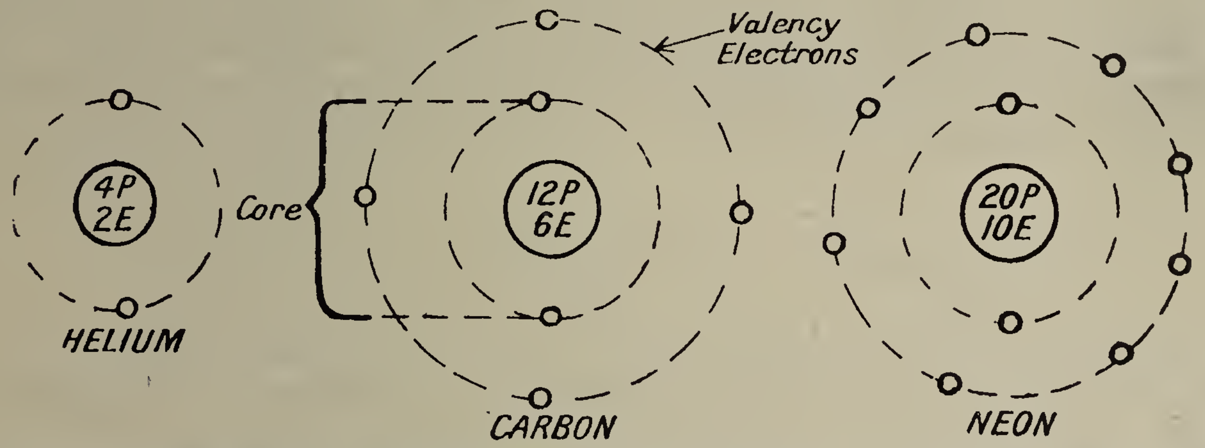


FIG. 9.—Diagrammatic representation of structure of helium, carbon and neon atoms (not to scale).

The nucleus + the *complete* shells of electrons surrounding it is known as the *core* of the atom : the electrons in the core take no part in chemical reactions. See Fig. 9.

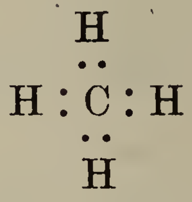
Kossel and Lewis assumed that the cause of chemical combination is the tendency of the electrons to redistribute themselves among the atoms combining so as to form the more stable arrangements which occur in the inert gases.

The atoms with which we are particularly concerned in organic chemistry are hydrogen, possessing but one electron, and carbon, nitrogen and oxygen, possessing respectively four, five and six valency electrons, in addition to two in the inner shell (and others in the nucleus). The hydrogen atom attempts to take up a more stable configuration either by giving up its electron and becoming a hydrogen ion, or by acquiring another and adopting the stable arrangement met with in helium. Carbon, nitrogen and oxygen tend to take up respectively four, three and two additional electrons, to form the stable octet possessed by the inert gas neon.

For example, hydrogen and chlorine combine to form hydrogen chloride, the hydrogen atom parting with its electron, which is then taken up by the chlorine atom, already possessing seven valency electrons, to complete the stable octet arrangement in its outer shell : the hydrogen thus acquires a positive charge and the chlorine a negative. This is an example of an ordinary ionized linking.

$$\mathrm{H}^{\cdot} + .\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}: \longrightarrow [\mathrm{H}]^{+}\left[:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:\right]^{-}$$

The atoms in the middle groups of the periodic table show less tendency to the formation of ionic links, and Lewis in the paper referred to made the suggestion that it was possible for an electron to be shared between two atoms, so as to contribute towards the stability of both. On this view, the electronic constitution of methane can be represented as

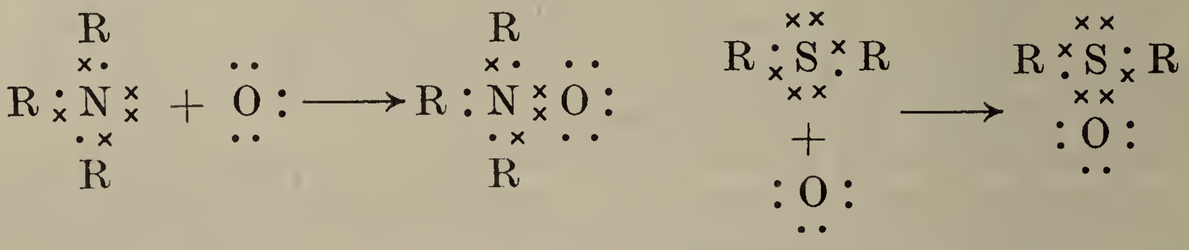


$$\begin{array}{c} \mathrm{H} \\ \cdot\cdot \\ \mathrm{H}:\mathrm{C}:\mathrm{H} \\ \cdot\cdot \\ \mathrm{H} \end{array}$$

one of the electrons in each bond being contributed by the hydrogen atom and the other by the carbon.

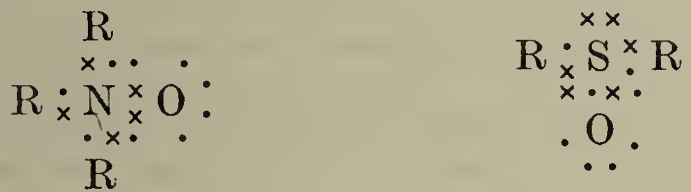
The above give examples of the two types of valency described by Langmuir as electrovalency and covalency, the electrovalency where one atom loses an electron to another atom, and the covalency where the two atoms mutually share two electrons, each contributing one.

So far this has done no more than replace an ordinary valency bond represented by a line by two dots representing two electrons, but Lewis put forward the new conception that it was possible for two atoms to share two electrons, both having been contributed by one atom. Thus compounds such as the sulphoxides or amine oxides can be represented as :



instead of by the ordinary formula with a double bond between sulphur or nitrogen and oxygen.

If the compounds are represented as containing an ordinary double bond, the nitrogen or sulphur atoms will be surrounded by a shell of ten electrons, which is a much less stable state than that of eight electrons. The formulæ of the compounds on the basis of an ordinary covalent double bond are given below. (In these formulæ and those above, the electrons contributed by the nitrogen or sulphur are indicated by a ×, those from other elements by · for clarity, but it must be clearly understood that when once the compound is formed, there is no distinction between the two electrons : the pairs ×· are held jointly by the two atoms and it cannot be said that × belongs to one and · to the other atom.) It should be noted that in both methods of formulation for the amine oxides or sulphoxides the total number of electrons is the same : the distribution alone is different.



Amine oxide. Sulphoxide.

(Represented as containing ordinary double bonds.)

The type of linkage where both electrons are contributed by one of the participating atoms is described as a co-ordinate covalency (Sidgwick) or a semipolar double-link (Lowry) and is conventionally represented by various symbols. Thus trimethylamine oxide may be represented as follows :

$$(CH_3)_3\overset{+}{N}-\overset{-}{O} \qquad (CH_3)_3N \mathrel{\overset{\rightharpoonup}{=}} O \qquad (CH_3)_3N \longrightarrow O$$

(I) (II) (III)

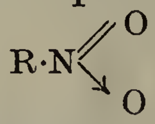
The symbol represented by (III) will be used in this book wherever it is necessary to refer to a co-ordinate link.

It may be suggested that this conception of a co-ordinate link is purely theoretical and has no basis in fact, but its assumption affords an explanation for certain phenomena inexplicable on the older views, and a consideration of the parachor (p. 77) gives strong evidence in support of the hypothesis.

A sulphoxide represented by the classical formula $\genfrac{}{}{0pt}{}{R}{R_1}\!>\!S=O$ should be incapable of optical activity, whereas the compound $CH_3{\cdot}SO{\cdot}C_6H_4COOH$ has actually been resolved by Harrison, Kenyon and Phillips (J.C.S. **1926**, 2079). If the compound is represented as containing a semipolar or co-ordinate link $\genfrac{}{}{0pt}{}{CO_2H{\cdot}C_6H_4}{CH_3}\!>\!S\longrightarrow O$ and the three sulphur valencies be assumed as directed towards three of the corners of a tetrahedron, this optical activity is to be expected.

Similarly, the amine oxides $R^1R^2R^3N\rightarrow O$ are resolvable when R^1, R^2 and R^3 are different, and this is readily explicable on the basis of a tetrahedral arrangement of the groups round the nitrogen atom.

If we compare an ionized compound with one containing only covalencies, the following contrasts are observed. The ionized compound is volatile only with difficulty, and is, in general, soluble only in solvents of a high dielectric constant, and its solution is a conductor of electricity. The covalent compound, on the other hand, is more volatile, soluble in liquids of low dielectric constant, such as benzene, and its solution is non-conducting. Further, a covalency, where the orbits of the two electrons are in some way jointly related to the two atoms may have a directional factor, thus accounting for the phenomena of stereoisomerism. An ionized link cannot have any directional effect and, in fact, the asymmetry of a tetraalkylammonium salt, $NR^1R^2R^3R^4X$, is due entirely to the four alkyl groups attached to the nitrogen, and is tetrahedral in arrangement, exactly like an asymmetric carbon atom.

In some ways compounds containing co-ordinate covalencies occupy a position intermediate between ionized and covalent compounds, particularly in respect of their volatility. A compound containing a co-ordinate link, such as a nitro compound  $R\cdot N\begin{smallmatrix}\nearrow O\\ \searrow O\end{smallmatrix}$ is much less volatile than an isomer containing only covalent links such as a nitrite, $R\cdot O\cdot N : O$, *e.g.* nitroethane boils at 114°, whereas ethyl nitrite boils at 17°.

Radicals, Residues, Groups.—Atomic complexes which remain unchanged through a series of reactions are referred to as radicals, residues or groups. According to their combining ability, one speaks of monovalent, divalent and trivalent radicals, the following examples being derived from methane :

CH_4	$—CH_3$	$=CH_2$	$\equiv CH$
Methane, saturated.	Methyl, univalent radical.	Methylene, divalent radical.	Methenyl or Methine, trivalent radical.

If such radicals are isolated from existing compounds, *e.g.* the halogen derivatives, then two of them unite to form a molecule :

$$\begin{array}{l} CH_3I \\ CH_3I \end{array} + 2Na = \begin{array}{l} CH_3 \\ | \\ CH_3 \end{array} + 2NaI$$

$$\begin{array}{l} CH_2I_2 \\ CH_2I_2 \end{array} + 4Cu = \begin{array}{l} CH_2 \\ \| \\ CH_2 \end{array} + 2Cu_2I_2$$

$$\begin{array}{l} CHCl_3 \\ CHCl_3 \end{array} + 6Na = \begin{array}{l} CH \\ ||| \\ CH \end{array} + 6NaCl$$

Or, an atomic rearrangement may occur with the production of a molecule of the same number of carbon atoms :

$$\begin{array}{l} CHCl_2 \\ | \\ CH_3 \end{array} + 2Na = \begin{array}{l} CH_2 \\ \| \\ CH_2 \end{array} \left(\text{instead of } \begin{array}{l} CH= \\ | \\ CH_2 \end{array}\right) + 2NaCl$$

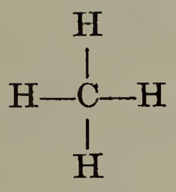
Evidence of the transitory existence of free radicals has recently been obtained. By heating tetraethyl lead at a low pressure in a stream of hydrogen, free ethyl is formed and yields volatile organic metallic compounds when passed over zinc, antimony, cadmium (Ber. **55**, 2889 : Ann. **446**, 31, 49 : Naturwissenschaften, 1930, **18**, 307 : Nature, 1930, **125**, 564). Free radicals are much more easily formed among the aromatic compounds : *cf.* triphenylmethyl, etc. (Vol. II) : see also tetraethylammonium (p. 187).

The expressions *residue* and *group* are similar to radical. They are chiefly applied to inorganic radicals, *e.g.* :

$—OH$	hydroxyl group,
$—SH$	sulphydryl group,
$—NH_2$	ammonia residue or amino group,
$=NH$	imino group,
$—NO_2$	nitro group,
$—NO$	nitroso group.

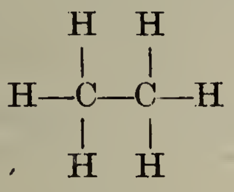
Homologous and Isologous Series.—Schiel, in 1842 (Ann. **43**, 107 : **110**, 141), directed attention to the phenomenon of homology, giving as evidence the alcohol radicals, and was followed shortly after by Dumas, who observed it in the fatty acids. Gerhardt introduced the terms *homologous* and *isologous series*, and showed the *rôle* these series played in the classification of the carbon derivatives. It was the theory of atomic linking that first disclosed the cause of homology.

The different kinds of linkages between the carbon atoms shows itself most plainly among the hydrocarbons. By removing one atom of hydrogen from the simplest hydrocarbon, methane, CH_4, the remaining univalent group, CH_3, can combine with another, yielding $CH_3—CH_3$, or C_2H_6, ethane or dimethyl. Here, again, a hydrogen atom may be replaced by the group CH_3, resulting in the compound $CH_3—CH_2—CH_3$, propane. The structure of these derivatives may be more clearly represented graphically :



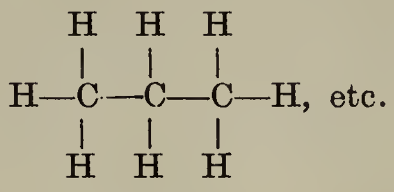
$$\begin{array}{c} H \\ | \\ H—C—H \\ | \\ H \end{array}$$

CH_4
Methane.



$$\begin{array}{c} H \quad H \\ | \quad\; | \\ H—C—C—H \\ | \quad\; | \\ H \quad H \end{array}$$

C_2H_6
Ethane.



$$\begin{array}{c} H \quad H \quad H \\ | \quad\; | \quad\; | \\ H—C—C—C—H, \text{ etc.} \\ | \quad\; | \quad\; | \\ H \quad H \quad H \end{array}$$

C_3H_3
Propane.

By continuing this chain-like union of the carbon atoms, there arises an entire series of hydrocarbons :

$CH_3—CH_2—CH_2—CH_3$ $\quad$ $CH_3—CH_2—CH_2—CH_2—CH_3$, etc.

C_4H_{10} Butane. $\quad$ C_5H_{12} Pentane.

Such a series of bodies of similar chemical structure and corresponding in chemical characters is known as a *homologous series.*

The composition of such a homologous series can be expressed by a general *empirical* or *rational* formula. The series formula for the marsh gas or methane hydrocarbons is C_nH_{2n+2}.

Each member differs from the one immediately preceding and the one following by CH_2. The phenomenon of homology is therefore due to the linking power of the quadrivalent carbon atoms.

Recently evidence has been obtained by physical methods, largely based on X-ray spectroscopy, that in many long carbon chains the carbon atoms are arranged in a zig-zag manner, the angle formed by three carbon atoms approximating to the tetrahedral angle, but sometimes diverging from it. See Proc. Physical Soc. **35**, 269 : J.C.S. **123**, 2043, 3152, 3156 : **1926**, 2310 : Nature, **119**, 50 : Z. physik. Chem. **128**, 203 : Proc. Roy. Soc. [A] **124**, 317 : J.C.S. **1929**, 234.

This zig-zag arrangement probably accounts for many of the examples of alternation of physical properties between odd and even members when ascending a homologous series.

In addition to the homologous series of the saturated marsh-gas type, there are a large number of other such series, of which the simplest are those of the monohydroxy-alcohols, the aldehydes and monocarboxylic acids.

	$C_nH_{2n+2}O$		$C_nH_{2n}O$		$C_nH_{2n}O_2$
CH_4O	Methyl alcohol	CH_2O	Formaldehyde	CH_2O_2	Formic acid
C_2H_6O	Ethyl alcohol	C_2H_4O	Acetaldehyde	$C_2H_4O_2$	Acetic acid
C_3H_8O	Propyl alcohol	C_3H_6O	Propionaldehyde	$C_3H_6O_2$	Propionic acid
$C_4H_{10}O$	Butyl alcohol	C_4H_8O	Butyraldehyde	$C_4H_8O_2$	Butyric acid
	etc.		etc.		etc.

Carbon compounds, chemically similar, but differing from each other in composition by a difference other than $n\mathrm{CH_2}$, *e.g.* the saturated and unsaturated hydrocarbons, form *isologous* series, according to Gerhardt:

$$\begin{array}{c}C_2H_6\ldots\ldots C_2H_4\ldots\ldots C_2H_2\\C_3H_8\ldots\ldots C_3H_6\ldots\ldots C_3H_4\end{array}$$

Isomerism; Polymerism; Metamerism.—The view once prevailed that bodies of different properties must necessarily possess a different composition. The first carbon compounds showing that this opinion was erroneous were discovered in 1820.

Liebig, in 1823, demonstrated that silver cyanate and fulminate were identical in composition. In 1828 *Wöhler* changed ammonium cyanate to urea, and in 1830 *Berzelius* established the similarity of tartaric acid and racemic acid, and designated as *isomers* (ἰσομερής, composed of similar parts) bodies of similar composition but different in properties. A year later he distinguished two kinds of isomerism, viz.: isomerism of bodies of different molecular mass—*polymerism*; and bodies of like molecular mass—*metamerism*: at the present time the term *isomerism* is usually restricted to the latter kind, and is usually employed in place of the term metamerism.

Numerous isomeric carbon derivatives were discovered in rapid succession; hence, an answer to the question as to what causes isomeric phenomena acquired importance for the development of organic chemistry. The deeper insight into the structure of carbon compounds, which was gradually attained, gave rise in consequence to a further division of metameric phenomena.

The expression *metamerism* was employed to designate that kind of isomerism which is due to the homology of radicals held in combination by atoms of higher valence. If the homologous radicals are joined by polyvalent elements, then those compounds are metameric, in which the sum of the elements contained in the radicals is the same (H may be viewed as the simplest radical):

$$\left.\begin{array}{r}C_2H_5\\H\end{array}\right\}O \quad \text{is metameric with} \quad \left.\begin{array}{r}CH_3\\CH_3\end{array}\right\}O$$

Ethyl alcohol. Methyl ether.

$$\left.\begin{array}{r}C_3H_7\\H\end{array}\right\}O \quad \text{is metameric with} \quad \left.\begin{array}{r}C_2H_5\\CH_3\end{array}\right\}O$$

Propyl alcohol. Ethylmethyl ether.

$$\left.\begin{array}{r}C_2H_5\\H\\H\end{array}\right\}N \quad \text{is metameric with} \quad \left.\begin{array}{r}CH_3\\CH_3\\H\end{array}\right\}N$$

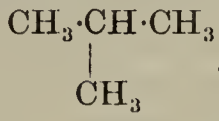
Ethylamine. Dimethylamine.

$$\left.\begin{array}{r}C_3H_7\\H\\H\end{array}\right\}N \quad \text{is metameric with} \quad \left.\begin{array}{r}C_2H_5\\CH_3\\H\end{array}\right\}N \quad \text{and} \quad \left.\begin{array}{r}CH_3\\CH_3\\CH_3\end{array}\right\}N$$

Propylamine. Ethylmethylamine. Trimethylamine.

The constitution of the radicals in this division was disregarded; the type formulæ were sufficiently explanatory. We have recognized the power of the quadrivalent carbon atoms to unite in a chain-like manner as the cause of homology, and to this cause may be attributed other phenomena of isomerism, which are not properly included under metamerism.

In deducing the formulæ of the five simplest hydrocarbons of the homologous series C_nH_{2n+2}, the formula for ethane, $CH_3\cdot CH_3$, was developed from that of methane, CH_4, and that of propane $CH_3\cdot CH_2\cdot CH_3$ from the formula of ethane C_2H_6. In the case of propane *intermediate* and *terminal* carbon atoms can be distinguished. The former are attached on either side to two other carbon atoms, still possessing two valency units which are saturated by two hydrogen atoms. The terminal carbon atoms of the chain are linked to three hydrogen atoms.

With the next member of the series we observe a difference. Above (p. 33), the fact that a hydrogen of the terminal methyl group of propane was replaced by methyl was the only condition considered. This led to the formula $CH_3\cdot CH_2\cdot CH_2\cdot CH_3$. However, the CH_3-group might replace a hydrogen atom of the intermediate CH_2-group, and then the result would be the formula  $\underset{\underset{\displaystyle CH_3}{|}}{CH_3\cdot CH}\cdot CH_3$. In this hydrocarbon there is a *branched* carbon chain. The hydrocarbon with a continuous chain is termed *normal butane*; its isomer is iso*butane*, *i.e. isomeric* butane.

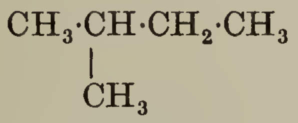
Theoretically, by a similar deduction, the two butanes

$CH_3—CH_2—CH_2—CH_3$
Normal butane.

$CH_3CH(CH_3)_2$
*iso*Butane.

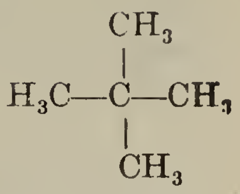
yield three isomeric pentanes which are actually known.

$CH_3\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_3$
Normal pentane.



$\underset{\underset{\displaystyle CH_3}{|}}{CH_3\cdot CH}\cdot CH_2\cdot CH_3$

*iso*Pentane.



$H_3C—\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}—CH_3$

Tetramethylmethane.

The number of possible isomers increases rapidly with the increase in carbon atoms (Ber. **27**, R. 725 : **33**, 2131).

The origin of isomerism in the homologous paraffins, as in so many other cases, is the different constitution of the carbon chain. The isomerism caused by a difference in linking, by the different structure of the carbon nucleus or the carbon chain, is termed *nucleus* or *chain isomerism.*

The investigation of the substitution products of the paraffin hydrocarbons brings to light another kind of isomerism. The principle of similarity of the four valences of a carbon atom (p. 24) renders possible but one monochloro-substitution product of methane and ethane. The same consideration which heretofore recognized the possibility of two methyl substitution products of propane (the two butanes possible by theory) leads to the possibility of two monochloropropanes, dependent upon whether the chlorine atom has replaced the hydrogen of a terminal or intermediate carbon atom :

$CH_3\cdot CH_2\cdot CH_2Cl$
Normal propyl chloride.

$CH_3\cdot CHCl\cdot CH_3$
*iso*Propyl chloride.

If two hydrogen atoms of one of the carbon atoms of propane be replaced by an oxygen atom, the following case of isomerism arises :

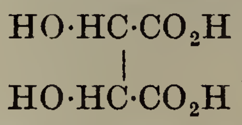
$CH_3{\cdot}CH_2{\cdot}CHO$ — Propionaldehyde.
$CH_3{\cdot}CO{\cdot}CH_3$ — Acetone.

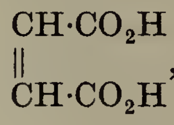
In the case of the two known chloropropanes, and also in the case of propionaldehyde and acetone, the cause of the isomerism is not due to difference in constitution of the carbon chain, but to the different *position* of the chlorine atoms with reference to the oxygen atoms of the same carbon chain. Isomerism, induced by the different arrangement or position of the substituting elements in the same carbon chain, is designated *place* or *position isomerism.*

STEREOISOMERISM

The theory of atomic linking not only revealed an insight into the causes of the innumerable isomeric phenomena, but predicted unknown instances and determined their number in a very definite manner. In many cases isomeric modifications, possible by theory, were discovered at a later period. For certain isomers, however, at first few in number, the structural formulæ deduced from their synthetic and analytical reactions were insufficient, inasmuch as different compounds were known, to which the same structural formula could be given. The greatest similarity in reactions indicative of the structure was combined with complete difference in physical properties of the compounds belonging in this class. The tendency at first was to designate such bodies *physical isomers*, meaning thereby an aggregation of varying complexes of chemically similar molecules.

The following groups of such isomers have been well investigated :

1. The *four symmetrical dihydroxysuccinic acids* :  $\begin{array}{c}HO{\cdot}HC{\cdot}CO_2H\\ |\\ HO{\cdot}HC{\cdot}CO_2H\end{array}$, the ordinary or *dextro*-tartaric acid, and racemic acid, which were proved to be isomeric in 1830 by *Berzelius* (see p. 34), and *lævo*-tartaric and the inactive or *meso*-tartaric acids which were added later, through Pasteur's classic researches.

2. The *two symmetrical ethylenedicarboxylic acids* :  $\begin{array}{l}CH{\cdot}CO_2H\\ \|\\ CH{\cdot}CO_2H\end{array}$, fumaric and maleic acid.

3. The *three α-hydroxypropionic acids* : $CH_3{\cdot}CH(OH){\cdot}CO_2H$— inactive lactic acid of fermentation, sarcolactic acid, and *lævo*-lactic acid, which was added later.

Substances are included among these compounds, which when liquefied, either by fusion or solution, rotate the plane of polarization either to the right or left. The direction of deviation is indicated by prefixing " dextro " or " lævo " or (+)- or (—)- to the name of the bodies thus acting. Such carbon compounds are " *optically active* " (p. 68), in contradistinction to the other almost innumerable derivatives which exert no influence on polarized light and are " optically inactive " or " inactive."

A direct synthesis of optically active carbon compounds has not yet been achieved except by the use of enzymes (Fermentforschung, **5,** 334 : see also asymmetric synthesis, p. 71), although optically inactive bodies have been synthesized. *Pasteur* discovered methods by means of which the latter can be resolved into their components, which rotate the plane of polarization to an equal degree but in opposite directions. Upon splitting sodium-ammonium racemate into sodium-ammonium *lævo-* and *dextro*-tartrates, Pasteur observed that the crystals of these salts showed hemihedrism ; that they were as an object to its mirror-image ; and that equally long columns of equally concentrated solutions of these salts, at the same temperature, deviated the plane of polarized light to an equal degree in opposite directions.

In 1860 Pasteur expressed himself as follows upon the cause of these phenomena—upon molecular asymmetry : " Are the atoms of the *dextro*-acid grouped in the form of a right-handed spiral, or *are they arranged at the angles of an irregular tetrahedron,* or are they distributed according to some other asymmetric arrangement ? We know not. Undoubtedly, however, we have to do with an asymmetric arrangement, the images of which cannot mutually cover each other. It is not less certain that the atoms of the *lævo*-acid are arranged in opposite order." In 1873 *J. Wislicenus* added the following comment to the evidence of similar structure in the optically inactive lactic acid of fermentation and the optically active sarcolactic acid : " Facts compel us to explain the difference of isomeric molecules of like structural formula by a difference in arrangement of the atoms in space." How the configuration in space of the molecules of carbon compounds was to be represented was answered almost simultaneously and independently of each other by *van 't Hoff* and *Le Bel* (1874) (Ber. **26,** R. 36), by the introduction of the hypothesis of the asymmetric carbon atom. This hypothesis is the basis of the chemistry of space or *stereo-chemistry* of the carbon atom.

The hypothesis of an *asymmetric carbon atom* * is designed to explain optical activity and the isomerism of optically active carbon compounds.

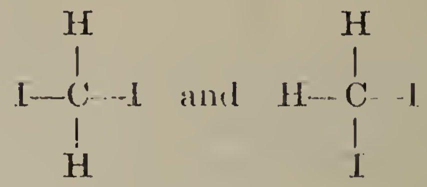
Whilst the theory of atomic linkage abstains from any representation of the spacial arrangement of the atoms in a molecule, experience gathered from the investigation of simple carbon compounds shows that definite spacial relations do not harmonize with actual facts. Assuming that the four valences of a carbon atom act in a plane and in perpendicular directions upon each other, the following possible isomers for methane are evident :

No isomers of the types CH_3R^1 and $CH(R^1)_3$
Two ,, ,, ,, $CH_2(R^1)_2$, $CH_2R^1R^2$, $CHR^2(R^1)_2$,
Three ,, ,, ,, $CHR^1R^2R^3$.

---

* *Pasteur :* Recherches sur la dissymétrie moléculaires des produits organiques naturels. Leçons de chimie professées en 1860. Paris, 1861. *J. H. van 't Hoff :* Dix années dans l'histoire d'une théorie, 1887. *K. Auwers :* Die Entwickelung der Stereochemie, Heidelberg ,1890. *A. Hantzsch :* Grundriss der Stereochemie, Breslau, 1893. *C. A. Bischoff :* Handbuch der Stereochemie, 1893, together with, Materialien der Stereochemie, 1904. *Werner :* Lehrbuch der Stereochemie 1904. *P. Walden :* Lecture, Ber. **58,** 237.

Methylene iodide, for example, should appear in two isomeric modifications

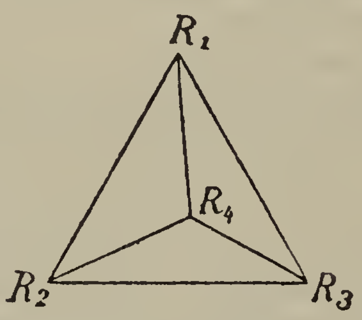


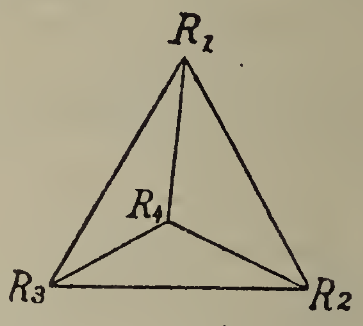
$$\begin{array}{c}H\\|\\I-C-I\\|\\H\end{array}\quad\text{and}\quad\begin{array}{c}H\\|\\H-C-I\\|\\I\end{array}$$

However, two isomers of a single disubstitution product of methane have never been found ; consequently, it is very improbable that the four affinities of a carbon atom are disposed in the manner indicated above. The carbon atom models of Kekulé represent the carbon atom as a black sphere and the quadrivalence of it by four needles of equal length and firmly attached to the sphere, which Baeyer has called axes. These needles are not perpendicular to each other, nor do they lie in the same plane, but are so arranged that planes placed about their terminals produce a regular tetrahedron (Z. f. Chem. (1867) N. F. 3, 216). *Van 't Hoff's* generalizations are based upon this model, about which fundamental considerations will be more fully developed in the following pages.

On the assumption that the affinities of a carbon atom are directed towards the summits of a regular tetrahedron, in the centre of which is the carbon atom, there would be no imaginable isomers coinciding with $CH_2(R^1)_2$, $CH_2R^1R^2$, $CHR^2(R^1)_2$, but a case such as $CHR^1R^2R^3$ or the more general $CR^1R^2R^3R^4$—an isomeric phenomenon of peculiar nature—might be predicted. A carbon atom of this description, connected with four different univalent atoms or atomic groups, van 't Hoff has designated an *asymmetric carbon atom.*

If a compound contains an asymmetric carbon atom we can conceive of its existence in two isomeric modifications, the one being an image of the other :





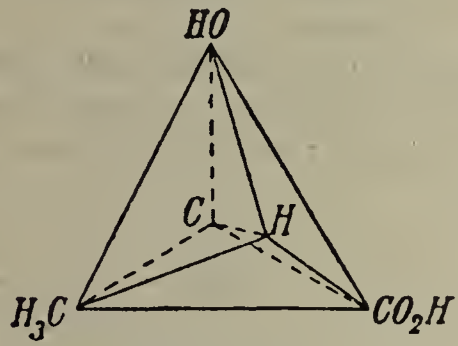
These spacial arrangements are more fully understood by the aid of the models suggested by Kekulé, van 't Hoff, and others, than by their projection upon the flat surface of paper. Van 't Hoff introduced tetrahedron models in which the solid angles were coloured ; this was to represent and indicate different radicals. They lack this advantage, possessed by the Kekulé model, that the carbon atom has entirely disappeared from the model. It must be imagined as being in the centre of the tetrahedron, and in projections of these models (see above) the radicals are united to each other by lines, the latter, however, not in any sense representing a chemical union.

In the left tetrahedron the successive series $R^1R^2R^3$ proceeds in a direction directly opposite to that of the hand of a watch, whilst in the right tetrahedron the course coincides with that of the hand. The two figures cannot, by rotation, be by any means brought into the same position—that is. in a position to cover each other completely

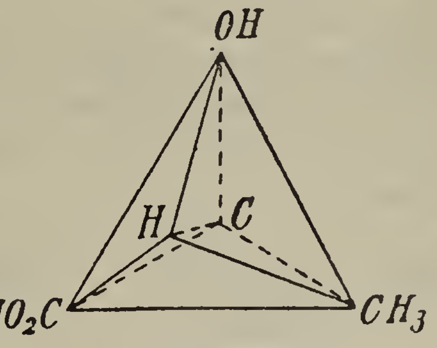
—any more than the left hand can be made to cover the right, or a picture its image or reflection.

The Isomerism of Optically Active Carbon Compounds.—The cause of optical activity, in the opinion of van 't Hoff and of Le Bel, is the presence of one or several asymmetric carbon atoms in the molecule of every optically active body. It is obvious that two molecules which only differ in that the series of atoms or atomic groups attached to an asymmetric carbon atom differ successively in order of arrangement, which therefore are identical in chemical structure, must be very similar in chemical properties. However, those physical properties, upon which the opposite successive series of atoms or atomic groups in union with asymmetric carbon exerts an influence, *e.g.* the power of deviating the plane of polarized light, must be equal in value, but opposite. The union of two molecules identical in structure, having equal but opposite rotatory power, gives rise to a molecule of an optically inactive polymeric compound.

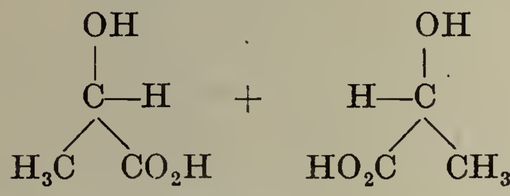
Compounds containing **one** *Asymmetric Carbon Atom.*—α-Hydroxypropionic acid, $CH_3 \cdot {*}CHOH \cdot CO_2H$, is an example of a compound containing one asymmetric carbon atom. It exists in two optically active, structurally identical, but physically isomeric modifications, and one optically inactive, structurally identical polymeric form :



dextro-Lactic acid.
(Sarcolactic acid.)

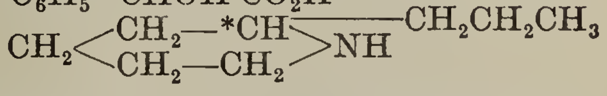


lævo-Lactic acid.



{ (+) R-Lactic Acid (−) L-Lactic Acid = } Lactic Acid of Fermentation or Inactive Lactic Acid.

The following compounds also contain one asymmetric carbon atom :

Leucine	$C_4H_9{*}CH(NH_2)CO_2H$
Malic Acid	$CO_2H \cdot CH_2 \cdot {*}CH(OH)CO_2H$
Asparagine	$CONH_2CH_2 \cdot {*}CH(NH_2)CO_2H$
Mandelic Acid	$C_6H_5 \cdot {*}CHOH \cdot CO_2H$
Coniine	 $CH_2\left<\begin{matrix}CH_2—{*}CH—CH_2CH_2CH_3\\ CH_2—CH_2\end{matrix}\right>NH$

Each of the preceding bodies is known in two optically active and one optically inactive modifications.

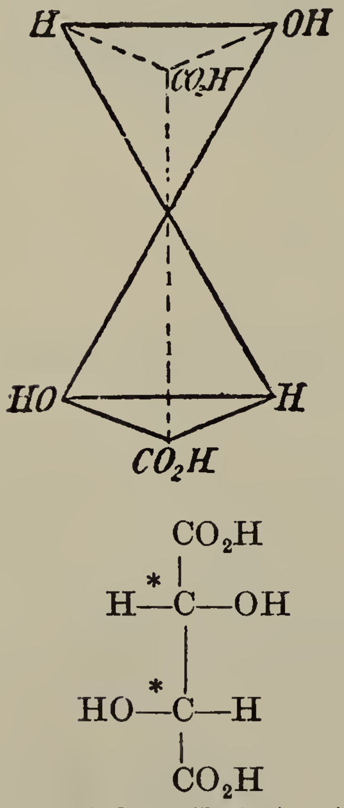
Compounds containing **two** *Asymmetric Carbon Atoms.*—The relations are more complicated when two asymmetric carbon atoms are present.

The simplest case would be that in which similar groups are in union with the two asymmetric carbon atoms. The one half of the molecule would then be constructed chemically exactly like the other half. The four isomeric dihydroxysuccinic acids belong in this group. This group of tartaric acids has become of the greatest importance in the development of the chemistry of optically active carbon derivatives.

They were the first to be most carefully investigated chemically, optically, and crystallographically, and were employed by *Pasteur* in the development of methods for resolving the optically inactive compounds into their optically active components (p. 72). Their importance was further increased by the fact that they were brought into an intimate relationship with fumaric and maleic acids—two isomeric bodies which will be considered in the next section (p. 41).

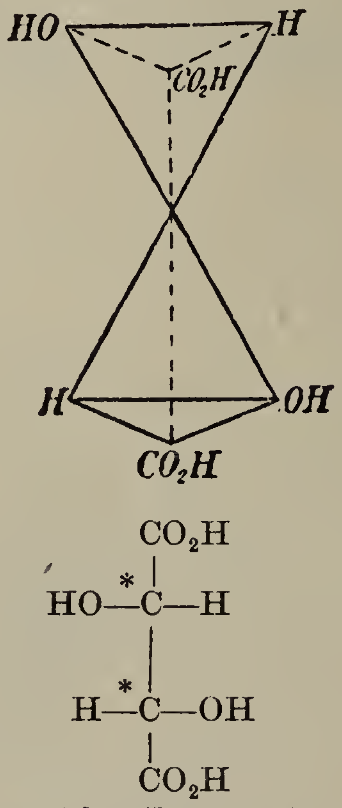
When a carbon compound contains two asymmetric carbon atoms, united to similar groups, then a fourth compound becomes possible in addition to the three isomeric modifications which a compound containing only one asymmetric carbon atom is capable of forming. If the groups linked to one asymmetric carbon atom, viewed from the axis of union of the two asymmetric carbon atoms, show an opposite successive arrangement to that of the other asymmetric carbon atom, an inactive compound results, due to an *intramolecular* or *internal compensation*; the action due to the one asymmetric atom upon polarized light will be cancelled by an equal but opposite action caused by the other asymmetric carbon atom.

The hypothesis of the asymmetric carbon atom gave the first and, indeed, the only satisfactory explanation for the occurrence of four isomeric symmetrical dihydroxysuccinic acids, which are represented as follows:



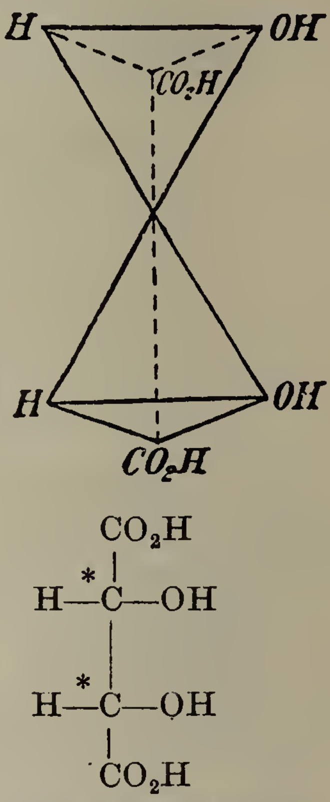
$$\begin{array}{c} CO_2H \\ | \\ H-\overset{*}{C}-OH \\ | \\ HO-\overset{*}{C}-H \\ | \\ CO_2H \end{array}$$

(1) *dextro*-Tartaric acid.



$$\begin{array}{c} CO_2H \\ | \\ HO-\overset{*}{C}-H \\ | \\ H-\overset{*}{C}-OH \\ | \\ CO_2H \end{array}$$

(2) *lævo*-Tartaric acid.



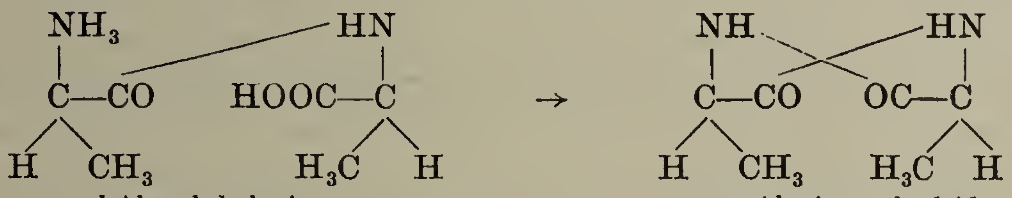
$$\begin{array}{c} CO_2H \\ | \\ H-\overset{*}{C}-OH \\ | \\ H-\overset{*}{C}-OH \\ | \\ CO_2H \end{array}$$

(3) Inactive or *meso*Tartaric acid.

dextro-Tartaric acid + *lævo*-Tartaric acid = (4) Racemic acid.

It is seen that the two independent rotating systems are in contact with one another at one angle of the tetrahedrons through a single carbon bond.

An excellent example of the formation of a meso-form by the combination of two optical antipodes, is supplied by *l*-alanyl-*d*-alanine. It is itself optically active, but loses water, giving rise to the *meso*-form of alanine anhydride (C. 1906, II. 59):



l-Alanyl-*d*-alanine. *meso*Alanine anhydride.

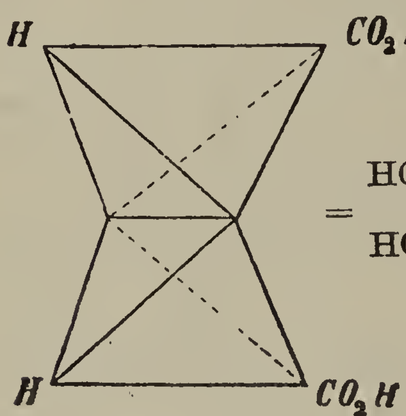
The possibilities of isomerism in carbon compounds containing more than two asymmetric carbon atoms—a condition observable with the polyhydric alcohols, their corresponding aldehyde alcohols, and ketone alcohols (the simplest sugar varieties), as well as with their oxidation products, will be more elaborately discussed under these several groups of compounds.

Geometrical Isomerism, Stereoisomerism of the Ethylene Derivatives (*Alloisomerism*).—Two carbon atoms, singly linked to each other, whose valences are not required for mutual union, and which are united to other atoms or atomic groups, may be considered as being able to rotate independently of each other about their axis of union. Wislicenus assumed, however, that the atoms or atomic groups combined with these two carbon atoms exercise a "directing influence" upon each other until finally the entire system has passed into the "*favourable configuration*" or the "*preferred position.*" It follows from this assumption that, in ethane derivatives in which asymmetric carbon atoms are not present, structurally identical isomers cannot occur. When the van 't Hoff tetrahedron models are employed for demonstration the two systems, capable of independent rotation about a common axis, are found to touch one another through a single carbon bond situated at one of the angles (comp. the projection-formula of the tartaric acids, p. 40).

A different state prevails where the carbon atoms are doubly linked. The double union, according to van 't Hoff, prevents a free and independent rotation of the two systems and space-isomers are possible. The tetrahedron models represent this double union in such a manner that two tetrahedra have two angles in common and are in contact along a common edge. The frequent and notable differences in chemical behaviour of this class of isomers are to be attributed to the greater or less spacial distance of the atomic groups, which determine the chemical character.

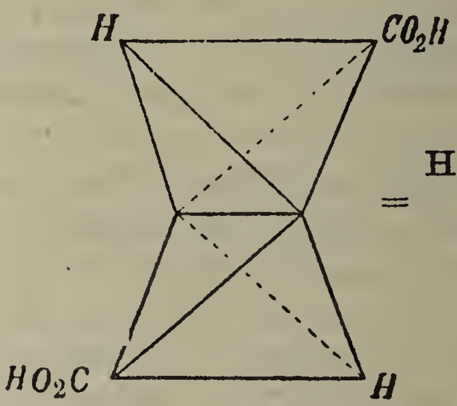
Compounds having the general formulæ $abC{=}Cab$ or $abC{=}Cac$, may exist in two isomeric modifications. In one instance groups of like name are directed towards the same side—according to Wislicenus the "*plane symmetrical configuration*"—or they are directed towards opposite sides—then they have according to the same author the "*central* or *axially symmetrical configuration.*" The plane-symmetric configuration is now usually referred to as the "*cis*" modification, the axially-symmetric as the "*trans.*" Baeyer suggests for this form of asymmetry the term "*relative asymmetry*" in contradistinction to the kind of asymmetry which substances with asymmetric carbon atoms show; the latter he prefers to call "*absolute asymmetry.*"

The structurally symmetrical ethylenedicarboxylic acid is the most striking example of this class of isomerism. It exists in two isomeric modifications, known as *fumaric* and *maleic acids*, both of which have been very carefully investigated. Maleic acid readily passes into an anhydride, hence the plane symmetrical configuration is ascribed to it; fumaric acid does not form an anhydride, so that the axial symmetrical configuration is given to it, in which the two carboxyl groups are as widely removed from each other as possible. In projection formulæ and in structural formulæ, to which there is given a spacial meaning, the configuration of these two acids would be represented in the following way:



$$= \begin{matrix} HC{\cdot}CO_2H \\ \| \\ HC{\cdot}CO_2H \end{matrix}$$

Maleic acid.
Plane Symmetrical Configuration.
cis-Configuration.



$$= \begin{matrix} HO_2C{\cdot}CH \\ \| \\ H{\cdot}CO_2H \end{matrix}$$

Fumaric acid.
Central or Axially Symmetrical Configuration.
trans-Configuration.

The isomerism of mesaconic and citraconic acids, $(CH_3)(CO_2H)C{=}CH(CO_2H)$, is of the same class; the first acid corresponds to fumaric acid and the second to maleic acid. Further examples of the class are:

Crotonic and *iso*Crotonic acids	$CH_3CH : CHCO_2H$.
Angelic and Tiglic acids	$CH_3{\cdot}CH : C(CH_3)CO_2H$.
Oleic and Elaidic acids	$C_8H_{17}CH : CH{\cdot}C_7H_{14}{\cdot}CO_2H$.
Erucic and Brassidic acids	$C_8H_{17}CH : CH{\cdot}C_{11}H_{22}{\cdot}CO_2H$.
The two α-Chlorocrotonic acids	$CH_3{\cdot}CH : CCl{\cdot}CO_2H$.
,, ,, β-Chlorocrotonic acids	$CH_3{\cdot}CCl : CH{\cdot}CO_2H$.
,, ,, Tolane dichlorides	$C_6H_5CCl : CClC_6H_5$.
,, ,, ,, dibromides	$C_6H_5CBr : CBrC_6H_5$.
,, ,, *o*-Dinitrostilbenes	$NO_2[2]C_6H_4[1]CH : CH[1]C_6H_4[2]NO_2$.
Cinnamic and Allocinnamic acids	$C_6H_5{\cdot}CH : CHCO_2H$.
The two α-Bromocinnamic acids	$C_6H_5{\cdot}CH : CBrCO_2H$.
,, ,, β-Bromocinnamic acids	$C_6H_5{\cdot}CBr : CHCO_2H$.
,, ,, Coumaric acids	$HO[2]C_6H_4[1]CH : CH{\cdot}CO_2H$, etc.

Isomeric phenomena of this kind Michael designates as *allo-isomerism,* without suggestion as to its cause. When a body passes into a more stable modification upon the application of heat, Michael prefixes "*allo*" to the name of the more stable form; thus, fumaric acid is allomaleic acid (Ber. **19,** 1384).

Fumaric and maleic acids are placed at the head of this class of isomeric phenomena not only because they have been most thoroughly investigated, but chiefly because the two optically inactive dihydroxytartaric acids bear to them an intimate genetic relation (p. 40). Kekulé and Anschütz showed that fumaric acid was converted into racemic acid, and maleic acid into *meso*tartaric acid by potassium permanganate. This conversion harmonizes entirely with the van 't Hoff-Le Bel conception of these four acids; indeed, it might have been predicted. These relations will be more fully elaborated in the discussion on the acids.

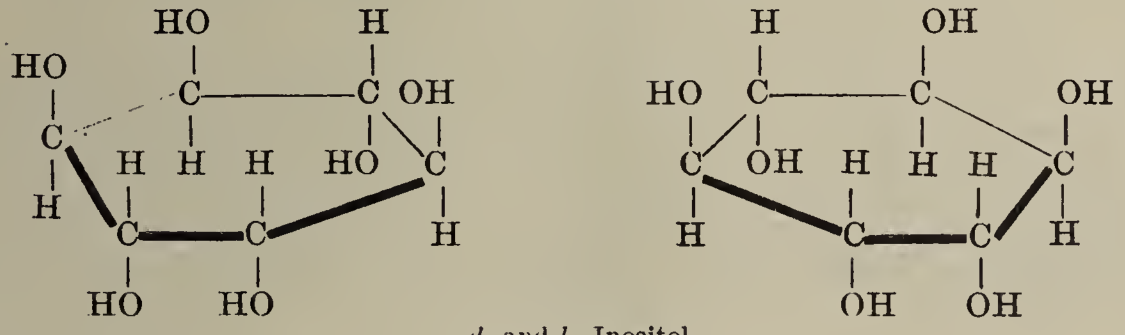
Baeyer considers that the isomerism of the saturated or carbocyclic compounds bears a definite relation to the stereoisomerism of the ethylene derivatives, as will be more fully explained when the hexahydroxyphthalic acids (Vol. II) are described. The same author maintains that the simple ring-union of carbon atoms viewed from a stereochemical standpoint has the same signification as the double union in open chains. Therefore, stereoisomerism in the carbon compounds with double union would appear merely as a special case of isomerism in simple ring-unions. Baumann applied this idea to saturated heterocyclic compounds—to the polymeric thioaldehydes (*q.v.*).

Baeyer suggested the introduction of a common symbol for all geometrical isomers, such as the Greek letter Γ. "The addition of an index will assist the ready expression of the kind of isomerism. In the case of compounds which contain absolute asymmetric carbon atoms, the signs + — can be employed. Thus the expressions

$$\left.\begin{array}{ll} \textit{dextro}\text{-Tartaric acid} & = \Gamma + + \\ \textit{lævo}\text{-Tartaric acid} & = \Gamma - - \\ \textit{meso}\text{Tartaric acid} & = \Gamma + - \end{array}\right\}\text{Tartaric acid}$$

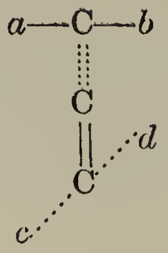
can be understood without special explanation." In the case of relative asymmetry in unsaturated compounds and saturated rings, Baeyer proposes to use the terms *cis* and *trans*. Maleic acid = $\Gamma^{\text{cis, cis}}$ or briefly *cis*-ethylenedicarboxylic acid, while fumaric acid = $\Gamma^{\text{cis, trans}}$ or *trans*-ethylenedicarboxylic acid.

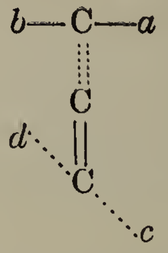
Further considerations on the space-configuration of the ethylene and polymethylene derivatives lead to a broadening of the scope and to the correction of the law, that an asymmetric carbon atom must be present in every optically active compound (see above, p. 38). Optical activity can occur even in the absence of an asymmetric carbon atom in the ordinary sense, *if the atoms are attached to a carbon skeleton in such a way in space, that there is no plane of symmetry present*—the object and its mirror-image do not correspond. This is found, for instance, in hexahydrohexahydroxybenzene, which exists in two enantiomorphic optically active forms, as *d*- and *l*- inositol:



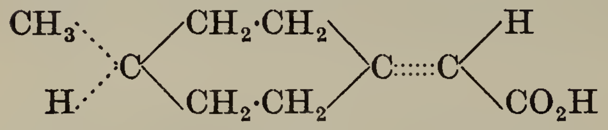
d- and *l*- Inositol.

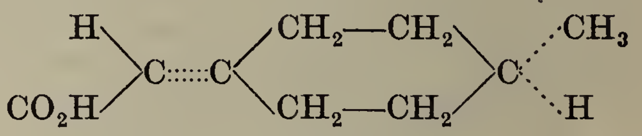
The same considerations apply to the *allene* compounds, *Cab* : C : *Ccd*. In virtue of the tetrahedral configuration of the groups attached to a carbon atom, the radicals *a*, *b* and *c*, *d* must be arranged in two planes perpendicular to each other. The following diagrams represent this asymmetry, the full lines being assumed to lie in the plane of the paper and the dotted lines in a plane at right angles to this.





The conditions are not altered if one or both of the ethylene linkages is replaced by a cyclic grouping. An example of this is the resolution of 4-methyl*cyclo*hexylideneacetic acid (*Marckwald*, Ber. **39,** 1171 : Ann. **371,** 180).





For stereochemical considerations of *spiran* compounds (in which one atom is simultaneously a member of two different rings), see Ber. **45,** 2114 : **47,** 2573.

The particularly ready formation of carbocyclic and heterocyclic compounds when five or six carbon atoms take part in the ring formation, is also a result of the position of the atoms in space. This aspect of stereochemistry will be considered in the introduction to the carbocyclic compounds, and there also to the heterocyclic bodies, as well as in the discussion of the cyclic carboxylic esters, or lactones, the cyclic acid amides or lactams, the anhydrides of dibasic acids, etc.

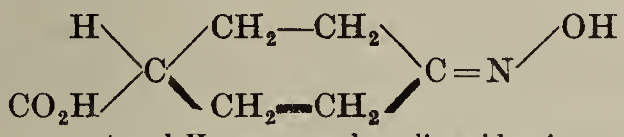
Hypotheses Relating to Multiple Carbon Bonds.—The multiple carbon bonds are so important in stereochemical considerations, that there has been a large amount of research into the nature of this union as well as attempts to represent it. All investigations in this direction demonstrate how difficult it is at present to understand so obscure a force as chemical attraction or affinity from a mechanical point of view. Despite the demand and necessity that may exist for the introduction of hypotheses dealing with the mechanics of multiple linkage the views so far presented are in many essentials contradictory, and not one has won general recognition for itself. See *Baeyer* (Ber. **18,** 2277 : **23,** 1274) ; *Wunderlich* (Configuration organischer Molecüle, Leipzig, 1886) ; *Lossen* (Ber. **20,** 3306) ; *Wislicenus* (Ber. **21,** 581) ; *V. Meyer* (Ber. **21,** 265 Anm. : **23,** 581, 618) ; *V. Meyer* und *Riecke* (Ber. **21,** 946) ; *Auwers* (Entwicklung der Stereochemie, Heidelberg, 1890), pp. 22–25 ; *Naumann* (Ber. **23,** 477) ; *Brühl* (Ann. **211,** 162, 371) ; *Deslisle* (Ann. **269,** 97) ; *Skraup* (Monatsh. **12,** 146) ; *J. Thiele* (Ann. **306,** 87 : **319,** 129) ; *Erlenmeyer, jun.* (Ann. **316, 43** ; J. pr. Chem. [2] **62,** 145) ; *Vorlaender* (Ann. **320,** 66) ; *Hinrichsen* (Ann. **336,** 168).

Stereochemistry of Nitrogen

Isomeric phenomena occur among nitrogen containing compounds of the same constitution, which cannot be referred to an asymmetric carbon atom, and compel the attribution of asymmetric properties to the nitrogen atom. If the organic ammonium salts are represented, after Werner, by the formula $\left[{}^{a}_{b}\mathrm{N}^{c}_{d}\right]\mathrm{X}$ where the radicals *a*, *b*, *c*, *d* are co-ordinatively attached to the central nitrogen atom and the anion X attached by an ionic linkage, the ammonium compounds can be compared with the compounds containing an asymmetric carbon atom $\left[{}^{a}_{b}\mathrm{C}^{c}_{d}\right]$. The theory of an asymmetric nitrogen atom was first substantiated by the resolution by Pope and Peachy in 1899 (J.C.S. **75**, 1127) of methylallylphenylbenzylammonium iodide $C_6H_5{\cdot}CH_2(CH_3)(C_3H_5)(C_6H_5)NI$. Other optically active quaternary ammonium iodides have been obtained subsequently (*cf. E. Wedekind*, Zur Stereochemie des fünfwertigen Stickstoffs, 2. Aufl. Leipzig, 1907). The resolution of a purely aliphatic ammonium compound has not yet been satisfactorily accomplished (J.C.S. **101**, 519 : Ber. **45**, 2940 : Ann. **428**, 253).

Meisenheimer has resolved methylethylaniline oxide, $C_6H_5NMeEt{:}O$ and other amine oxides into their optical components (Ber. **41**, 3966 : Ann. **385**, 117 : **397**, 273 : **399**, 371) (Resolution of purely aliphatic amine oxides, see Ann. **428**, 252). This optical activity is readily understandable as due to tetrahedral asymmetry if the oxygen is regarded as attached to the nitrogen by a co-ordinate linkage, as in the formula $RR'R''N\rightarrow O$ (see p. 31).

The actual spatial arrangement of the groups round a trivalent nitrogen atom is not known : all attempts to resolve compounds containing trivalent nitrogen, derivatives of ammonia, hydrazine and hydroxylamine, have been unsuccessful (Ber. **57**, 1744). Evidence obtained by the study of compounds containing a double linked nitrogen atom such as oximes (*Hantzsch* and *Werner*, Ber. **23**, 11), hydroxamic acids (*Werner*) and diazo compounds (*Hantzsch*) leads to the view that the three valencies do not lie in one plane. The resolution of the oxime of 4-*cyclo*hexanonecarboxylic acid by Mills and Bain in 1910 (J.C.S. **97**, 1866) can only be explained by the assumption of a non-planar arrangement for these bonds.



4-*cyclo*Hexanonecarboxylic acid oxime.

Stereochemistry of Phosphorus.—Ber. **44**, 356 : **45**, 2933.

Stereochemistry of Arsenic.—J.C.S. **119**, 426 : **127**, 2479 : Ber. **58**, 2000.

Stereochemistry of Sulphur.—*Thionium salts*, J.C.S. **77**, 1072, 1174 : *sulphinic esters*, J.C.S. **127**, 2552 : *sulphoxides*, Ber. **44**, 756 : J.C.S. **1926**, 2079 : **1927**, 1798 : *sulphilimines*, J.C.S. **1927**, 188. Many of the above compounds, which exhibit tetrahedral type of symmetry, involve a semipolar (co-ordinate) double bond affecting the sulphur atom.

Stereochemistry of Selenium.—C. 1903, I. 22, 144.

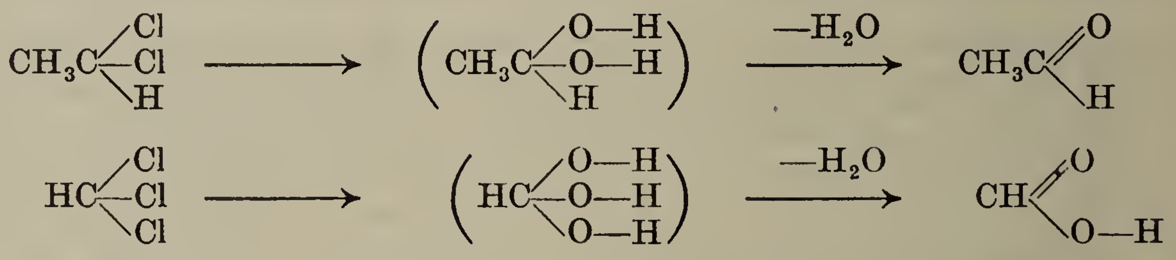
Stereochemistry of Tellurium.—J.C.S. **117**, 86, 889 : **119**, 105, 687 . **1929**, 560. See also dimethyltelluronium iodide (p. 178).

Stereochemistry of Tin.—C. 1900, II. 34.

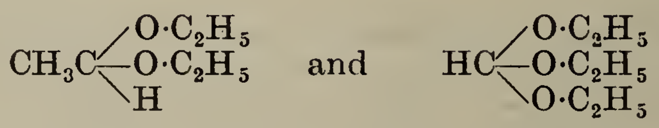
Stereochemistry of Silicon.—C. 1908, I. 1688 : 1909, I. 360 : 1910, I. 2083.

INTRAMOLECULAR ATOMIC REARRANGEMENTS

Many investigations have shown that certain modes of linking, apparently possible from a valence standpoint, cannot, in fact, occur, or when they do take place are possible only under certain definite conditions. In reactions, for example, in which two or three hydroxyl groups should unite with the same carbon atom, a loss of water almost invariably occurs and oxygen becomes doubly united with carbon, *e.g.* :

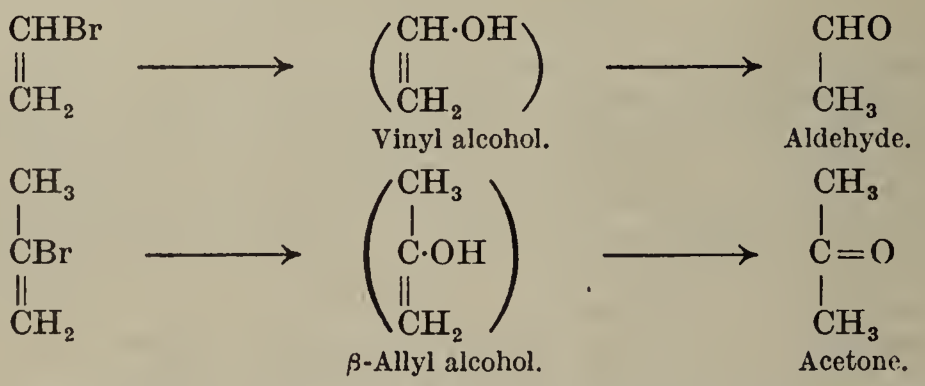


On the other hand, the ethers derivable from these unstable "alcohols" are stable :



In other cases there is a cleavage of a halogen hydride, water or ammonia, with the production of an unsaturated body, or an anhydride of a dibasic acid, or a cyclic ester (*lactone*), or a cyclic amide (*lactam*). In these reactions two molecules result from one molecule, in which atom-groups occur in unstable linkage-relations, an organic molecule and a simple inorganic body.

This type of decomposition of a labile molecule is similar to the intramolecular atomic rearrangements which occur where unstable atomic groupings pass at the moment of their formation into stable forms without the alteration of the size of the molecule. The hydrogen atom, especially, is inclined to wander, but groups, such as the alkyl, phenyl, and hydroxyl behave similarly. To-day, the number of examples of this phenomenon is remarkably large, of which a few only need be cited. A free hydroxyl group becomes added in most cases to a carbon atom in double union with its neighbouring carbon atom. When intramolecular atomic rearrangements occur the hydrogen of the hydroxyl attaches itself to the adjacent carbon atom, and oxygen of hydroxyl unites doubly with carbon (*Erlenmeyer's rule*, Ber. **13**, 309 : **25**, 1781).



However, the ethers obtained from vinyl alcohol (*q.v.*) are stable : $CH_2{=}CHO{\cdot}C_2H_5$ and $CH_2{=}C(O{\cdot}C_2H_5){-}CH_3$ are known.

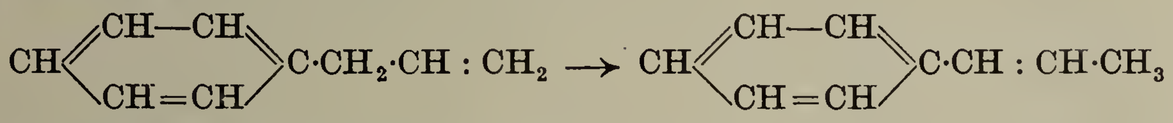
A further, very widely represented class of intramolecular migrations is the change of a compound with separated double bonds into an isomer containing a conjugated system. $\beta\gamma$-Unsaturated acids, for example, change into the $\alpha\beta$-unsaturated compounds.

$$\mathrm{CH_2:CH{\cdot}CH_2{\cdot}\underset{OH}{C}:O} \longrightarrow \mathrm{CH_3{\cdot}CH:CH{\cdot}\underset{OH}{C}:O}$$

Vinylacetic acid. Crotonic acid.

Itaconic anhydride. Citraconic anhydride.

Allylbenzenes are isomerized under the action of alkalis into the isomeric propenylbenzenes (see Vol. II).



Transformations of this type are particularly common among the terpene derivatives (Vol. II).

That these changes are due to the transformation of a labile compound into a more stable isomer is shown by the determination of the heats of combustion.

In some cases, the migration of an alkyl group instead of a hydrogen atom is observed. Examples are :

The esters of hydrothiocyanic acid, under the influence of heat, rearrange themselves into the isomeric mustard oils, sulphur unites doubly with carbon and the alcohol radical that had previously been in union with the sulphur wanders to nitrogen :

$$\mathrm{C_3H_5{-}S{-}C{\equiv}N} \longrightarrow \mathrm{S{=}C{=}N{\cdot}C_3H_5}$$

Allyl thiocyanate. Allyl mustard oil.

*iso*Nitriles or carbylamines, when heated, pass into nitriles ; the alcohol radical previously in union with nitrogen, wanders to carbon :

$$\mathrm{C_6H_5{-}N{=}C} \longrightarrow \mathrm{C_6H_5{-}C{\equiv}N.}$$

Phenylcarbylamine. (Vol. II.) Benzonitrile. (Vol. II.)

Trisubstituted acetaldehydes are partially isomerized by the action of concentrated sulphuric acid into disubstituted ketones (Compt. rend. **182**, 67).

$$\mathrm{R_3C{\cdot}CHO} \longrightarrow \mathrm{R_2CH{\cdot}CO{\cdot}R.}$$

O-Allylacetoacetic ester is changed by distillation in the presence of ammonium chloride into the *C*-alkyl derivative.

$$\mathrm{CH_3{\cdot}C(OC_3H_5):CH{\cdot}COOEt} \longrightarrow \mathrm{CH_3{\cdot}CO{\cdot}CH(C_3H_5){\cdot}COOEt.}$$

Among the characteristic transformations of the aromatic series are the isomerizations of amines and phenols substituted on the *N*- and *O*-atoms into their nuclear substituted isomerides (Vol. II).

$$\mathrm{C_6H_5{\cdot}NH{\cdot}OH} \longrightarrow \mathrm{HO{\cdot}C_6H_4{\cdot}NH_2}$$

Phenylhydroxylamine. *p*-Aminophenol.

$$\mathrm{C_6H_5{\cdot}NH{\cdot}NH{\cdot}C_6H_5} \longrightarrow \mathrm{NH_2{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}NH_2}$$

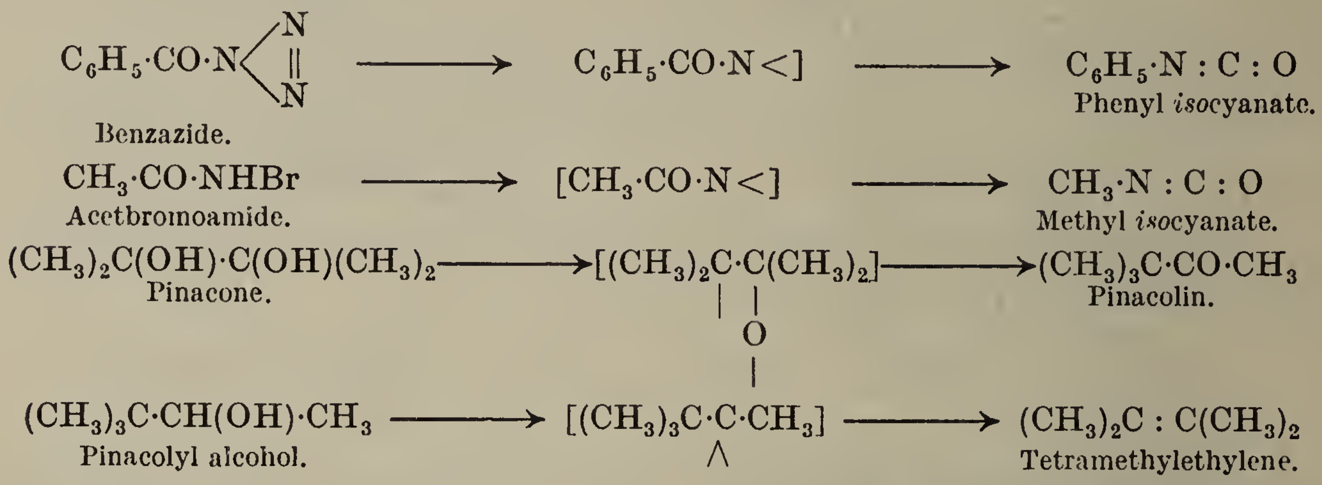
Hydrazobenzene. Benzidine.

$$\mathrm{C_6H_5{\cdot}O{\cdot}C_3H_5} \longrightarrow \mathrm{C_3N_5{\cdot}C_6H_4{\cdot}OH}$$

Phenyl allyl ether. *o*-Allylphenol.

All the transformations hitherto considered consist in a change from a relatively labile atomic conformation to a more stable isomer.

The following reactions depend upon the conversion of a stable substance, by loss of water, halogen acid, nitrogen, etc., into a compound unstable from the valency standpoint, which spontaneously changes into a stable form.



$$C_6H_5{\cdot}CO{\cdot}N_3 \longrightarrow C_6H_5{\cdot}CO{\cdot}N{<}] \longrightarrow C_6H_5{\cdot}N : C : O$$

Benzazide. Phenyl *iso*cyanate.

$$CH_3{\cdot}CO{\cdot}NHBr \longrightarrow [CH_3{\cdot}CO{\cdot}N{<}] \longrightarrow CH_3{\cdot}N : C : O$$

Acetbromoamide. Methyl *iso*cyanate.

$$(CH_3)_2C(OH){\cdot}C(OH)(CH_3)_2 \longrightarrow [(CH_3)_2C{\cdot}C(CH_3)_2] \longrightarrow (CH_3)_3C{\cdot}CO{\cdot}CH_3$$

Pinacone. Pinacolin.

$$(CH_3)_3C{\cdot}CH(OH){\cdot}CH_3 \longrightarrow [(CH_3)_3C{\cdot}C{\cdot}CH_3] \longrightarrow (CH_3)_2C : C(CH_3)_2$$

Pinacolyl alcohol. Tetramethylethylene.

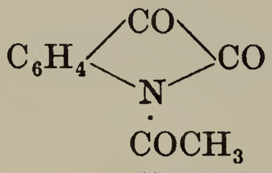
To this type of reaction belong in all probability the *benzilic acid transformation* (Vol. II), the *Beckmann inversion* of the ketoximes and other reactions.

Tautomerism, Desmotropy, Allelotropy, Pseudomerism, Ring-chain tautomerism

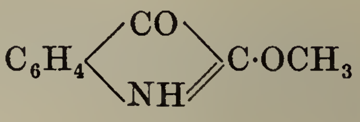
(*Cf. W. Wislicenus*, Ahrens Sammlung, **2**, 188 (1898): *Henrich*, Theorien der organischen Chemie, Braunschweig, 1924, Vieweg.).

The phenomena referred to under the names tautomerism and desmotropy include some of the most interesting intramolecular changes.

Baeyer in 1882 (Ber. **15**, 2093: **16**, 2193) obtained from isatin by the action of acetic anhydride an acetyl derivative, which must have the constitution (I). By the action of methyl iodide on the silver salt of isatin he obtained a methyl ether which should be represented by the formula (II):

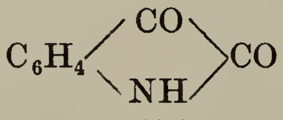


(I)

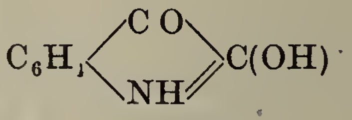


(II)

This led him to expect the occurrence of two forms of isatin which may be represented by (III) and (IV):



(III)



(IV)

All attempts to prepare these two forms of isatin by the removal of substituents failed. The same isatin was always obtained.

The number of compounds to which must be attributed, from a consideration of their derivatives, two structural formulæ increased rapidly from this time (Ber. **16**, 1704, 2188: **17**, 317, 2387, 2873, 2903: **18**, 1528). Compounds containing the following groups, in particular, show this phenomenon:

$$—CO{\cdot}NH— \longrightarrow —C(OH) : N— \qquad —CO{\cdot}CH_2— \longrightarrow C(OH) : CH—$$

$$—CH_2{\cdot}NO_2 \longrightarrow —CH : NO{\cdot}OH.$$

Baeyer recognized that the origin of this was the abnormal mobility of a hydrogen atom.

The classical example of tautomerism is acetoacetic ester. The formula $CH_3\cdot CO\cdot CH_2\cdot COOEt$ must be ascribed to the compound on the basis of its decomposition to acetone, the formation of *C*-mono- and di-alkyl derivatives by the action of alkyl halides on its sodium derivatives, and its behaviour towards the ketone reagents phenylhydrazine, hydroxylamine, etc. On the other hand, a series of reactions such as the formation of *O*-acetyl derivative by the action of acetyl chloride in pyridine solution leads to the recognition of the β-hydroxycrotonic ester formula $CH_3\cdot C(OH) : CH\cdot COOEt$. This ester, therefore, presents a typical example of a compound which reacts in two forms, and to which cannot be ascribed a definite constitutional formula.

In explanation of these phenomena, *Laar* (*cf. Butlerow*, Ann. **189**, 77 : *van 't Hoff*, Ansichten über die organische Chemie, 2, 263 and *Zincke*, Ber. **17**, 3030) suggests that such compounds consist of a mixture of structural isomers, in which a hydrogen atom oscillates between two equilibrium positions, and the whole complex acquires mobility therefrom. This conception of Laar, by which it is impossible to assign any definite constitution to the compound, is not of general application. Cases were soon met with in which both forms could be isolated (*Claisen*, Ann. **291**, 25 : *Wislicenus*, Ann. **291**, 147). The true cause of the phenomenon was put forward independently by Claisen and Wislicenus as an equilibrium between the two possible forms.

$$—C(OH) : CH— \quad \rightleftarrows \quad —CO\cdot CH_2—$$

$$—N : C(OH)— \quad \rightleftarrows \quad —NH\cdot CO—$$

The phenomenon will here be referred to by the name tautomerism, suggested by von Laar, which may be more accurately defined as follows (*K. H. Meyer*, Ann. **398**, 64).

Tautomerism.—Compounds are designated tautomeric when they form two series of derivatives, derived from two isomeric formulæ which differ from each other by the position of a hydrogen atom and one or more double bonds.

Desmotropy and pseudomerism are subdivisions of tautomerism.

Desmotropy.—Compounds are designated desmotropic when the two forms can be separately isolated, or at any rate separately detected.

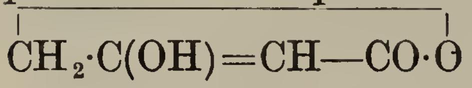
Pseudomerism.—When only one form of a tautomeric compound is known, pseudomerism is spoken of. The other form (*pseudo*-form) cannot be isolated and every test for its existence is unsuccessful. Here, one form yields by addition or substitution the derivatives of both forms.

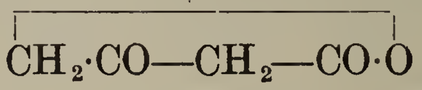
Desmotropic isomers are stable only in the solid state. In the liquid or gaseous form, or in solution, they change to an equilibrium mixture of the two, and form a so-called allelotropic mixture.

Early references to various types of tautomeric phenomena: *P. Jacobson*, Ber. **20**, 1732, footnote : **21**, 2628, footnote : *L. Knorr*, Ann. **303**, 133 : *Hantzsch*, Ber. **20**, 2802 : **21**, 1754 : *Förster*, Ber. **21**, 1857 : *Michael*, Ber. **27**, 2128, footnote : J. pr. Chem. [2] **45**, 581, footnote : **46**, 208.

The most important class of substances showing tautomerism consists of compounds containing the grouping $—CO·\underset{\bullet}{C}H·CO—$ which readily changes to the grouping $—C(OH):\underset{\bullet}{C}·CO—$, and the latter equally readily to the former.

If the usual name denotes the acid form, then that of the *pseudo*-acid is prefixed by the word *pseudo*-, as, for example,


$CH_2·C(OH)=CH—CO·O$ is called tetronic acid, and

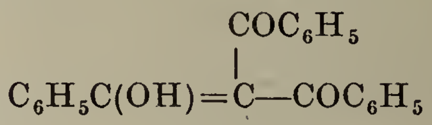

$CH_2·CO—CH_2—CO·O$

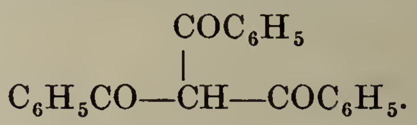
is *pseudo*-tetronic acid.

The system of nomenclature proposed by *Hantzsch* for pseudomeric substances (Ber. **38**, 1000) appears to be most suited for its purpose. If the accustomed name refers to the weaker acid or neutral form, then the name of the real acid is characterized by the prefix *aci*-. *Claisen* was the first to show that, in the above example of the two tribenzoyl methanes, only compounds having the *aci*- constitution form salts direct; the *pseudo*-form yields no salts, but gradually changes when in contact with bases, into the salt of the *aci*-form, *e.g.*:

$C_6H_5·CH_2·NO_2$	$C_6H_5·CH:NOOH$
Phenylnitromethane.	*aci*-Phenylnitromethane.

Claisen designates the acidic *enol*-form the α-compound and the neutral *keto*-form the β-body, *e.g.*:

α-Tribenzoylmethane 
$$C_6H_5C(OH)=\overset{\displaystyle COC_6H_5}{\overset{|}{C}}—COC_6H_5$$

β-Tribenzoylmethane 
$$C_6H_5CO—\overset{\displaystyle COC_6H_5}{\overset{|}{C}H}—COC_6H_5.$$

This reaction proceeds with a measurable velocity, affording thereby one of the criteria of a keto-enol tautomeric substance.

The following methods have been used successfully in the estimation of the proportions of enol and keto forms in a mixture.

1. Colorimetric estimation by means of ferric chloride (Ann. **291**, 179: Ber. **44**, 2725, 2772).
2. Titration of the enol form with bromine (Ann. **380**, 216) or thiocyanogen (Ber. **57**, 928, 934).
3. Titration of the enol with iodide-iodate (Ann. **335**, 1).
4. Estimation of the enol as copper salt (Ber. **54**, 902).
5. Physical methods:
    - (*a*) Determination of the molecular refraction (J. pr. Chem. [2], **50**, 119: Ber. **38**, 1668: **44**, 3514: Ann. **415**, 169).
    - (*b*) Determination of the molecular magnetic rotation (W. H. Perkin, senior).
    - (*c*) By the absorption spectra (Ber. **43**, 3049: **44**, 1771).
    - (*d*) Electrical conductivity (Ber. **33**, 2912: **39**, 2089, 2265, 3149).

Systematic investigation has shown that the equilibrium reached in a keto-enol tautomeric mixture is dependent upon:

1. Temperature (*Wislicenus*, Ann. **291**, 179)
2. Constitution of the compound. The following table gives the percentage of enol in various compounds (*cf.* also Ber. **45**, 2843: **55**, 2470).

Compound.	Enol %.	Compound.	Enol %.
$CH_2(COOEt)_2$	0	$C_6H_5·CO·CH_2·COOEt$	29·2
$CH(COOEt)_3$	0·2	$EtOCO·CO·CH_2·COOEt$	88
$CH_3·CO·CH_2·COOEt$	7·4	$CH_3·CO·CH_2·CO·CH_3$	76
$CH_3·CO·CHMe·COOEt$	3·1	$CH_3·CO·CH(COOEt)_2$	64

3. The nature of the solvent. The following table gives the enol percentage in about 3–5 per cent. solution.

Solvent.	Temp.	Acetoacetic Ester.	Benzoylacetic Ester.	Acetyl-acetone.
Water	0°	0·4	0·8	19
Glacial acetic acid	20°	5·7	14	74
Chloroform	20°	8·2	15·3	79
Ethyl alcohol	0°	12·7	26	84
Benzene	20°	18	31	85
Hexane	20°	48	69	92

A relation exists between the solubility of the two desmotropic forms and their equilibrium (van 't Hoff-Dimroth). The concentration of the two forms at equilibrium in a solution is equal to the ratio of their solubilities, multiplied by a constant G, which is a characteristic for each pair of tautomeric substances, and is independent of the solvent.

$$\frac{C_{\mathrm{Enol}}}{C_{\mathrm{Keto}}} = \frac{S_{\mathrm{Enol}}}{S_{\mathrm{Keto}}} \cdot G.$$

As the equilibrium between two tautomeric substances is directly dependent upon the rapidity of transformation of one form into the other, the above relationship brings out a close connection between speed of isomerization and solubility (Ann. **377,** 527 : **380,** 229 : **399,** 91 : Ber. **47,** 826).

It has already been mentioned that the salts of tautomeric compounds are always derived from the enol form. When these salts are treated with alkyl or acyl halides, a mixture of derivatives of both forms is produced, that of the keto form predominating, *e.g.* :

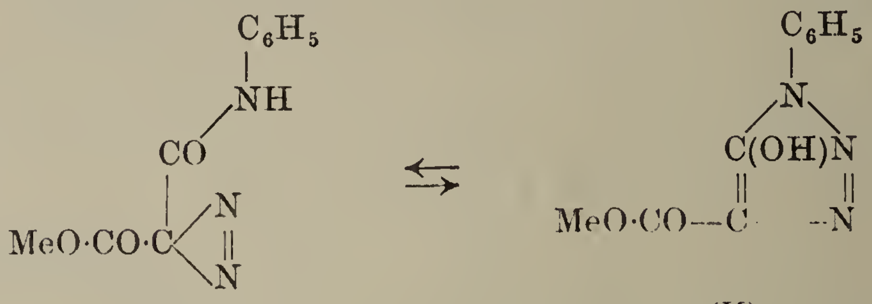
$$CH_3{\cdot}C(ONa) : \dot{C}H{\cdot}COOEt + MeI \longrightarrow CH_3{\cdot}CO{\cdot}CHMe{\cdot}COOEt + NaI.$$

Michael (J. pr. Chem. [2] **37,** 473) explains this reaction by the assumption that in the reaction between the salt and the alkyl halide, two independent reactions take place simultaneously. One of these consists in a simple exchange, whereby the entering group occupies the same position as the metal atom it has displaced. The other consists in a previous addition of the alkyl halide to the sodium derivative, followed by splitting off of sodium halide, the entering alkyl group under these conditions taking up a position different from that of the metallic atom. For further consideration of this mechanism, see under acetoacetic ester and malonic ester. Michael's view has recently been supported by Nef. (*cf.* lecture by Wislicenus, Z. angew. Chem. **1921,** 257).

A number of other reactions of desmotropic compounds, such as their coupling with aromatic diazo compounds (Ber. **40,** 2404, 4460 : **41,** 4012), their condensation with aldehydes and with *p*-nitrosodimethylaniline are to be explained in a similar manner. Investigations on the separate desmotropic compounds have shown that in these reactions the enol form alone reacts. The products are, however, derivatives of the keto form (Ann. **398,** 49, 66).

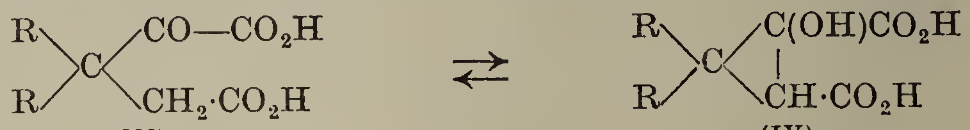
In a number of cases the transition from keto to enol form is not brought about merely by the migration of a hydrogen atom, but the opening or closing of a ring is also involved. The phenomenon is then described as ring-chain tautomerism.

An example of this given by Dimroth consists in the isomerization of the anilide of diazomalonic ester (I) to hydroxyphenyltriazolecarboxylic ester (II)



(I) (II)

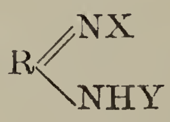
More recently the isomerization of the compounds (III) to the ring systems (IV) have been investigated by English workers.



(III) (IV)

(See J.C.S. **121**, 1765: **123**, 327, 1683, 2865, etc.)

In all the cases which have been considered, the interchangeable isomers have belonged to two different classes of compounds with quite different chemical characteristics. There exist, however, substances which according to their mode of preparation should give rise to two forms belonging to the same class, but which have turned out to be identical with one another, as, for example, diazoamino-compounds, amidines, formazyl derivatives of the general type—



and

where R represents N in diazoamino bodies, CH in the amidines, and N : CH·N in the formazyl derivatives. This explains the absence of certain isomerism phenomena in pyrrole, and such azoles as pyrazole and triazole (see Vol. III), and also in the ortho-di-derivatives of benzene (Vol. III, the Constitution of Benzene), etc. Attempts have been made to explain these phenomena by assuming oscillations of valences (*Knorr*, Ann. **279**, 188); this is further complicated, in the case of pyrrole and the azoles, by the wandering of a H atom. For the phenomenon itself Brühl suggests the name *Phasotropism* (Ber. **27**, 2396), whilst V. Pechmann puts forward the term *virtual tautomerism* (Ber. **28**, 2362).

Chromoisomerism, Polychromy, Pantochromy.—Hantzsch designated by the term *chromoisomerism* the property first observed in the cases of pyridine, quinoline and phenylacridine, of forming with acids or alkyl halides, salts of different colour, which are in equilibrium with each other, and which are frequently mutually interconvertible. When more than two differently coloured isomers occur, the phenomenon is referred to as *polychromy* or *pantochromy*. In addition to the compounds already mentioned, this type of isomerism also occurs among the dinitroparaffins, the nitro- and *iso*nitrosoketones (violuric acid), the nitrolic acids (ethylnitrolic acid) and other compounds. In many cases the explanation can be found in a variation of linkage, such as the following in the *iso*nitrosoketones :

$$—C(:NOH)\cdot CO— \rightleftarrows —C(\cdot NO):C(OH)—.$$

In these cases the phenomenon is simply due to tautomerism.

This explanation is insufficient in the case of polychromic compounds. In them, Hantzsch attributes the colour variations to the presence and differing activity of the subsidiary valencies (*cf.* Ber. **42**, 68, 966 : **43**, 82 : **44**, 1783, 3290 : **50**, 1204, 1719 : **52**, 1544).

Halochromy.—The term *halochromy* (Baeyer) refers to the property of certain organic substances, themselves colourless or faintly coloured, to combine with acids or heavy metal salts with the formation of highly coloured salts, without any appreciable structural change occurring.

The classical example of this is triphenylcarbinol, a colourless compound which dissolves in concentrated sulphuric acid with a golden yellow colour. According to Baeyer's view, this is due to the development by the central carbon atom of an ionized linkage, a so-called *carbonium* linkage, which he represented by a wavy line (Ber. **38**, 570 : **39**, 2977).

$(C_6H_5)_3C\cdot OH$
Triphenylcarbinol
Colourless.

$(C_6H_5)_3C \sim\!\sim O\cdot SO_3H$ or $[(C_6H_5)_3C]^+ [O\cdot SO_3H]^-$
Triphenylcarbinyl sulphate
Coloured.

More recent views (C. 1917, II. 357 : Wizinger, Z. angew. Chem. 1927, **40**, 939) attribute the development of halochromy to the weak attachment (partial valency) of the acid to the triphenylcarbinol or triphenylchloromethane as a molecular compound (*q.v.*). Through this unsymmetrical addition, a redistribution of valency takes place, leading to the development of a single strongly unsaturated central atom, denoted by the arrow, which acts as a strong chromophore.

$$(C_6H_5)_3C\cdot Cl + A \longrightarrow (C_6H_5)_3\underset{\downarrow}{C}\cdot Cl \; . \; . \; . \; A$$

The numerous highly coloured addition compounds of unsaturated ketones with halogen acids and heavy metal chlorides belong to the same class (*cf.* molecular compounds, p. 26) (*cf.* also Stobbe, Ann. **370**, 93, and the section on colour and constitution of organic compounds).

PHYSICAL PROPERTIES OF THE CARBON COMPOUNDS

The physical, as well as the chemical, properties of the carbon compounds are largely conditioned by their chemical constitution. A relationship between constitution and properties has been established for certain properties. The following physical properties are of importance for external characterization of a carbon compound :

1. Crystalline form.
2. Specific gravity.
3. Melting point.
4. Boiling point.
5. Solubility.

The following properties are of importance in the determination of the constitution of carbon compounds.

6. Optical properties :
    (*a*) Colour (Absorption of light).
    (*b*) Refraction.
    (*c*) Dielectric constant.
    (*d*) Optical rotatory power.
    (*e*) Magnetic rotatory power.
7. Electrical conductivity.
8. Parachor.

1. CRYSTALLINE FORM OF CARBON COMPOUNDS

The crystalline form of a carbon derivative is one of its most important distinctions, whereby a body may be recognized most definitely and differentiated from other substances (*cf. P. Groth*, Chemische Kristallographie, Bd. III, Leipzig, 1910) ; so that the preparation of organic substances in the form of crystals and their examination has been of the greatest value in organic chemistry. The more complex the constitution of a substance, the less the symmetry of its crystals (Ber. 27, R. 843). *The crystalline forms of isomeric bodies are always different.* Many substances may assume two or more forms ; they are *dimorphous*, *polymorphous*, but each is characterized very definitely by particular conditions of formation and existence.

When it is possible for a compound to crystallize from the same solvent in different forms, only one can separate within definite ranges of temperature. The limit between these zones, the *transition temperature*, is theoretically expressed by the point of intersection of the solubility curves of the two crystalline forms. It is only the one or the other form that can appear under normal conditions above or below this temperature. From a solution supersaturated as regards the two forms, it is possible by the introduction of one or the other form, to obtain each of the two kinds of crystals, and, indeed, both together, but only so long as the supersaturation continues. After that, one of the two forms will gradually dissolve and that one will remain which is the more stable at the temperature of experiment. The temperature of transformation varies for each solvent, and when impurities are present in the substances a greater or less variation in the temperature will occur, according to the degree of impurity.

The existence and stability of a definite modification of a polymorphic substance depends to a great extent on the temperature, of which the influence, however, is not always the same. In the case of perchlorethane C_2Cl_6, rhombic, triclinic, and regular crystal forms are successively assumed during a gradual rise in temperature, whilst on cooling, the same series is passed through in reversed order. The change is said, therefore, to be *reversible*, and polymorphic substances of this kind are called *enantiotropic* (*Lehmann*). With other bodies, however, one modification may be labile and the other stable, so that the first form changes into the second, and not vice versa. As an example, *p*-nitrophenol $C_6H_4(OH)NO_2$ may be taken. On solidification from the molten state, or from a hot solution, it crystallizes in the colourless labile form. This, on standing, turns into the stable yellowish-red modification, which is quite different in its cleavage and optical properties from the first. It can also be obtained by crystallizing from a cold solution. Such substances, which undergo a change in one direction only, are called *monotropic*. In many cases, however, a rigid grouping of the numerous polymorphic organic bodies in one or other of the two groups is not always easy. For the assumptions necessary for the explanation of the phenomenon, see *Zincke* (Ann. 182, 244) and *Lehmann* (Molekularphysik, Leipzig, 1888–89) ; *Graham-Otto* (Lehrbuch der Chemie, Vol. I, Part 3, p. 22, 1898).

At the present time little is known about the inner connection between the crystalline form and chemical constitution of carbon compounds, but it has been found, for example, that the slightest variation in chemical constitution does affect the amount of rotation exhibited by optically active compounds. Many such substances possess a hemihedral form, and the two optically active modifications of a carbon compound, although they exhibit the same geometrical constants, are distinguished by peculiar left and right types (*enantiomorphous forms*); they are not superposable. The difference between two such compounds, in which the atoms are similarly united, is only due, according to the hypothesis of an asymmetric carbon atom (p. 37), to the difference in arrangement of the atoms within the molecule. From this it follows that this variation in arrangement finds expression in the crystalline form (comp. Ber. **29**, 1692).

Laurent, Nicklès, de la Provostaye, Pasteur, Hjortdahl (see F. N. Hdw. **3**, 855) investigated the influence that chemical relations of organic bodies exerted upon the geometrical properties of their crystals. This problem, however, first appeared in the forefront of crystallographic study after P. Groth introduced the idea of *morphotropy* (Pogg. Ann. **141**, 31). By this term was understood the phenomenon of regular alteration of crystalline form produced by the entrance of a new atom or group in place of hydrogen. Groth, Hintze, Bodewig, Arzruni, and others frequently called attention to such morphotropic relations particularly with the aromatic bodies (comp. Physikal. Chemie der Krystalle von *Andreas Arzruni*, 1893).

The view put forward by Bravais (1848), and later developed by Wiener, Sohncke and particularly by Schönfliess, that the structure of crystals can be based upon a regular space-lattice has meanwhile received experimental confirmation. Pfeiffer, from the standpoint of the co-ordination theory, has arrived at the conclusion that there exists in crystals an absolutely regular arrangement of atoms or groups (Naturwissenschaften, 1920, **8**, 984).

For the elucidation of the fine structure of crystals, we are indebted to the methods of X-ray spectroscopy introduced and perfected by M. von Laue, W. H. and W. L. Bragg and P. Debye (*cf. M. v. Laue*, lecture, Ber. **50**, 8: Z. Krystallog. **52**, 58: Physikal. Z. **18**, 291). The investigation of the crystal structure of diamond and graphite (Physikal. Z. **18**, 291), which according to Debye represent the fundamental types for aliphatic and aromatic compounds respectively, is of the greatest importance for organic chemistry. For the use of X-ray spectroscopy in the determination of constitutional problems, see Ber. **61**, 612. See p. 33 for references to the use of X-rays in the study of the configuration of carbon chains.

2. SPECIFIC GRAVITY OR DENSITY

By this term is understood the relation of the absolute weight of a substance to the weight of an equal volume of a standard body. Conventional units of comparison are water for solids and liquids, and air or hydrogen for gaseous bodies (see p. 13).

Density of Gaseous Bodies.—For these, as we have already seen, the relation of the specific gravity (gas density) to the chemical composition is very simple. Since, according to Avogadro's law, an equal number of molecules are present in equal volumes, the gas densities stand in the same ratio as the molecular weights. Being referred to hydrogen as unit, the gas densities are one-half the molecular weights. Therefore, the *molecular volume*, *i.e.* the quotient of the molecular weight and specific gravity, is a constant quantity for all gases (at like pressure and temperature). Practical methods for repeated gas density measurements, see Pollitzer, Z. angew. Chem. **37**, 459.

Density of Liquid and Solid Carbon Derivatives.—In the liquid and solid states the molecules are considerably nearer each other than when in the gaseous condition. The size of the molecules and their distance from each other, which increases in different degrees with rise of temperature, are unknown, so that the theoretical bases for deducing the specific gravity are lacking. However, some regularities have been established empirically, which, by comparison with the specific or molecular volumes, give the ratio of molecular weight to specific gravity.

Kopp (Ann. **64**, 212 : **92**, 1 : **94**, 237, etc.) considered that the molecular volume was a purely additive property obtained from the separate atomic volumes, but Lossen and his collaborators and other workers (Ann. **214**, 81, 138 : **221**, 61 : **224**, 56 : **225**, 249, 316 : **243**, 1) have not confirmed this. More recent investigations (Kaufmann, Z. Elektrochem. **25**, 343) have failed to find a simple relation between molecular volume and constitution : there appears to be a diminution of molecular volume of 2·56 per double linkage in unsaturated compounds or cyclic compounds (Chem. News, **116**, 97).

Herz (Z. physik. Chem. **101**, 54) finds a relation between the molecular volume and molecular refraction at the boiling point of simple aliphatic compounds, the former being five times the latter.

Schroeder determined the specific volumes of a number of solids (Ber. **10**, 848, 1871 : **12**, 567, 1613 : **14**, 21, 1607, etc.).

In determining the specific gravity of liquid compounds, a small bottle—a *pyknometer*—is used, of which the narrow neck carries an engraved mark. More complicated apparatus, such as that designed by Brühl, based on Sprengel's form, is employed where greater accuracy is sought (Ann. **203**, 4) (Fig. 10). Descriptions of modified pyknometers will be found in Ladenburg's Handwörterbuch, **3**, 238. A convenient form by Ostwald is described in J. pr. Chem. **16**, 396. To obtain comparable results, it is recommended to make all determinations at a temperature of 20° C., and refer these to water at 4° and a vacuum. If m represents the weight of substance, v that of an equal volume of water at 20°, then the specific gravity at 20° referred to water at 4° and a vacuum (with an accuracy of four decimals), may be ascertained by the following equation (Ann. **203**, 8) :

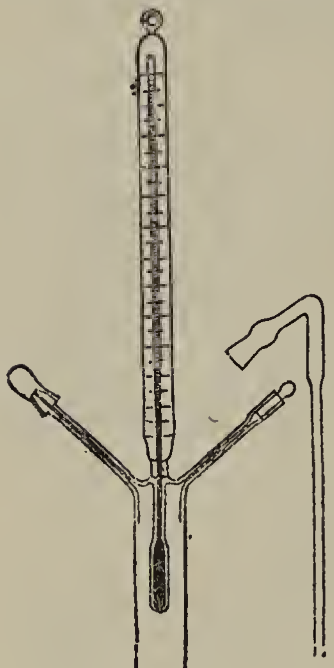


FIG. 10.

$$d_{4°}^{20°} = \frac{m.0{\cdot}99707}{v} + 0{\cdot}0012.$$

To find the specific volumes at the boiling temperature, the specific gravity at some definite temperature, the coefficient of expansion and the boiling point must be ascertained ; with these data the specific gravity at the boiling point is calculated, and by dividing the molecular weight by this, there results the *specific* or *molecular volume*. Kopp's dilatometer (Ann. **94**, 257 : Thorpe, J.C.S. **37**, 141 : Weger, Ann. **221**, 64), is employed in obtaining the expansion of liquids. For a method of obtaining the direct specific gravity at the boiling point, see Ramsay (Ber. **12**, 1024), Schiff (Ann. **220**, 78 : Ber. **14**, 2761), Schall (Ber. **17**, 2201), Neubeck (Z. physik. Chem. **1**, 652).

Kanonnikow, as well as Kopp and his followers, employed the " true density " in his calculations, not the figure as found directly. This he took as being the reciprocal of Lorenz's refraction constant, since, according to the Clausius and Mosotti theory, it constitutes the fraction of the total volume of a body which is actually occupied by the molecules themselves (C. 1899, II. 858 : 1901, I. 1190).

3. MELTING POINT

Every pure compound, if at all fusible or volatile, exhibits a definite melting temperature. It is customary to determine this for the characterization of the substance, and as a test of its purity. The melting point of a pure compound is not changed by recrystallization.

The slightest impurities frequently lower the melting point very considerably, and when foreign substances are present in larger amounts the melting point is irregular and not well defined—*i.e.* there is not a definite melting point. If two different substances have the same melting point, a mixture of them will show a considerably lowered melting point. The converse of this is of importance when establishing the identity of two bodies—the mixture must have the same melting point as each of the separate substances. Pressure influences the melting point to a very slight degree.

In some crystalline carbon compounds a double melting point is observed. When heated, the substance first melts to a doubly refracting, turbid " crystalline liquid " (L_1), which becomes clear and isotropic at a higher temperature (L_2, the " clearing point "). On cooling, the reverse order of changes may be observed :

$$\text{Solid crystals} \overset{L_1}{\rightleftarrows} \text{“ Crystalline liquid ”} \overset{L_2}{\rightleftarrows} \text{Amorphous liquid.}$$

The phenomenon apparently depends on chemical constitution, and is observed mainly in aromatic compounds, chiefly acids, acid esters, ketones, and phenolic ethers containing an azo- or azoxy- group. It is also shown by many cholesterol derivatives. (See *Vorländer*, Kristallinisch flüssige Substanzen, Stuttgart, 1928 : Theory of liquid crystals, see Physik. Zeitschr. 9, 708 : **10**, 32, 230 : **12**, 61, 837).

Determination of the Melting Point.—The most accurate method would be to immerse the thermometer in the molten substance ; this, however, would require large quantities of material (*Landolt*, Ber. **22**, R. 638).

Ordinarily, a small quantity of the finely pulverized material is introduced into a capillary tube closed at one end, which is attached to a thermometer, for instance, by a thin platinum wire, in such a way that the thermometer and capillary tube are on the same level. Alternatively, the substances may be pressed between two cover glasses (C. 1900, I. 241). A beaker containing sulphuric acid or liquid paraffin is used to furnish the heat, which is kept uniform throughout the liquid by agitation with a glass stirrer. A long-necked flask, containing sulphuric acid, is sometimes employed, in which a test tube is inserted or fused : in the latter case it is necessary that the flask should be provided with a side-tubulure (Fig. 11) (Ber. **10**, 1800 : **19**, 1971 : Am. Chem. J. **5**, 337 : C. 1900, II. 409). For other and more sensitive melting-point apparatuses, see *Houben*, Methoden der organischen Chemie, 1921, Bd. I, 727 *seqq.*

When the mercury thread of the thermometer extends far above the surface of the bath, it is necessary, in accurate determinations, to introduce a correction, by adding the value $n(T - t)$ 0·000154 to the observed point of fusion, where n is the length of the mercury column projecting beyond the bath expressed in degrees of the thermometer, T is the observed temperature, and t the temperature registered in the middle of the projecting portion of the mercury column ; 0·000154 is the apparent coefficient of expansion of mercury in glass (Ber. **22**, 3072 : Literature and Tables). After the melting point has been approximately determined with an ordinary thermometer a more accurate determination may be made by introducing a shorter thermometer, divided into fifths, with a scale carrying a limited number of degrees (about 50°).

The lack of agreement between the melting points of the same compound as determined by different workers, is often sufficient to prevent identification. This is not so much due to the thermometers as to the manner in which the determination is made. By rapid heating the mercury of the thermometer will not have time to assume the fusion temperature. In the region of the melting point the heat must be moderated so that during the course of the fusion the thermometer rises very slowly. Far more concordant figures might be obtained if a general use of short-scale thermometers were adopted and the time agreed upon for the mercury of the thermometer to rise through one degree of the scale during the observation.

Determination of low melting points, using an *air thermometer*, see Ber. **26**, 1052 : using a *thermocouple*, see Ber. **33**, 637. Apparatus for melting points below — 100°, see Ber. **50**, 156.

Determination of high melting points, see Ber. **28**, 1629 : **60**, 811 : J. pr. Chem. **116**, 291 : at red heat, Ber. **27**, 3129.

Melting point of coloured compounds, Ber. **8**, 687 : **20**, 3290.

Regularities in Melting Points.—(1) In the case of isomers it has been observed that the member possessing the most symmetrical structure generally shows the highest melting point ; for instance, among the aromatic series, *para*-compounds melt at a higher temperature than *ortho*- or *meta*-compounds. (2) Of the alkyl esters of the carboxylic acids those with the methyl residue have a higher melting point than that of the next homologues (see oxalic esters). (3) In homologous series with like linkages the melting point alternately rises and falls (see saturated normal aliphatic mono- and dicarboxylic acids, Ber. **29**, R. 411 ; C. 1900, I. 749). The members, having an uneven number of carbon atoms, have the lower melting points (*Baeyer*, Ber. **10**, 1286). This is also true of acid amides having from 6 to 14 carbon atoms (Ber. **27**, R. 551), and for the normal primary diamines (C. 1900, II. 1063 : 1901, I. 610, etc. : Z. physik. Chem. **50**, 43). (4) In the case of the benzene nitro-compounds and their derivatives—the azoxy-, azo, hydrazo-, and amino- bodies—as well as the corresponding diphenyl compounds, it has been observed that as oxygen is withdrawn the melting point rises until the azo-derivatives are reached, when it descends to the amino-bodies (*G. Schultz*, Ann. **207**, 362). To all these regularities among melting points there exist numerous exceptions (*Graham-Otto*, Lehrbuch der Chemie, Vol. I, part 3 (1898), p. 505 : *Franchimont*, C. 1897, II. 256). For the melting points of mixtures, see Ber. **29**, R. 75.

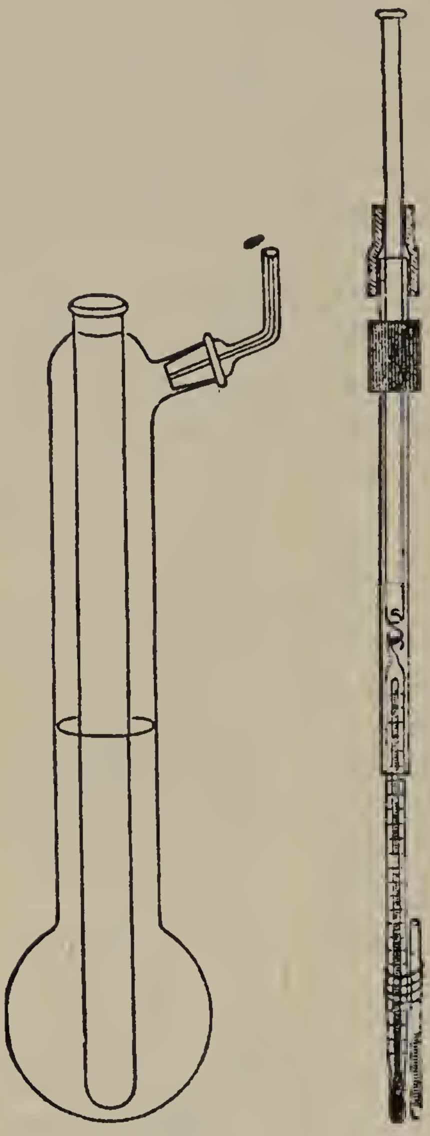


FIG. 11.

4. BOILING POINT ; DISTILLATION

The boiling points of carbon derivatives, which are volatile without decomposition, are as important for the purpose of characterization as the melting points. In case of the latter the influence of pressure is so slight that it can be neglected, but the former vary very markedly when small changes in pressure occur. Hence in stating a boiling point accurately it is necessary to add the pressure at which it was observed. When the quantity of material is ample the boiling point is determined by distillation. For the determination of the boiling points of very small amounts of liquids, see Ber. **24**, 2251, 944 : **19**, 795 : **14**, 88 : Monatsh. **38**, 219.

Distillation under Ordinary Pressure.—For this purpose a special flask is employed, the long neck of which is provided with a side tube pointing downwards at an angle. The neck of the flask is closed with a stopper, bearing a thermometer. It must not be forgotten that very frequently the vapours of organic substances attack ordinary corks or those of rubber, therefore the exit tube should be placed a considerable distance from the end of the neck ; or the neck may be narrowed at the upper end and the thermometer held in position by means of a piece of india-rubber tubing passed outside it. The mercury bulb of the thermometer should be slightly below the level of the exit tube in the neck of the flask. The latter should be at least one-half filled with the liquid to be distilled.

If the thermometer is not wholly immersed in the vapour, the exposed part of the scale will not be heated to the same temperature as that exposed to the vapour, hence the recorded temperature will be less than the true one. The necessary correction is the same as that which has already been given for the melting point. By using a shorter thermometer with a scale not exceeding 50°, which can be wholly surrounded by the vapour, the correction becomes unnecessary.

In general, when the boiling point " under ordinary pressure " is recorded, it is understood to mean at 760 mm. of mercury. If the barometric column does not indicate this amount during the distillation, a second correction is necessitated (Ber. **20**, 709; *Landolt-Boernstein*, Tabellen, 5th edition, 1923, p. 177). To avoid this it is possible to adjust the pressure in the apparatus to the normal, for which purpose the regulators of *Bunte* (Ann. **168**, 139) and *Lothar Meyer* (Ann. **165**, 303) are suitable.

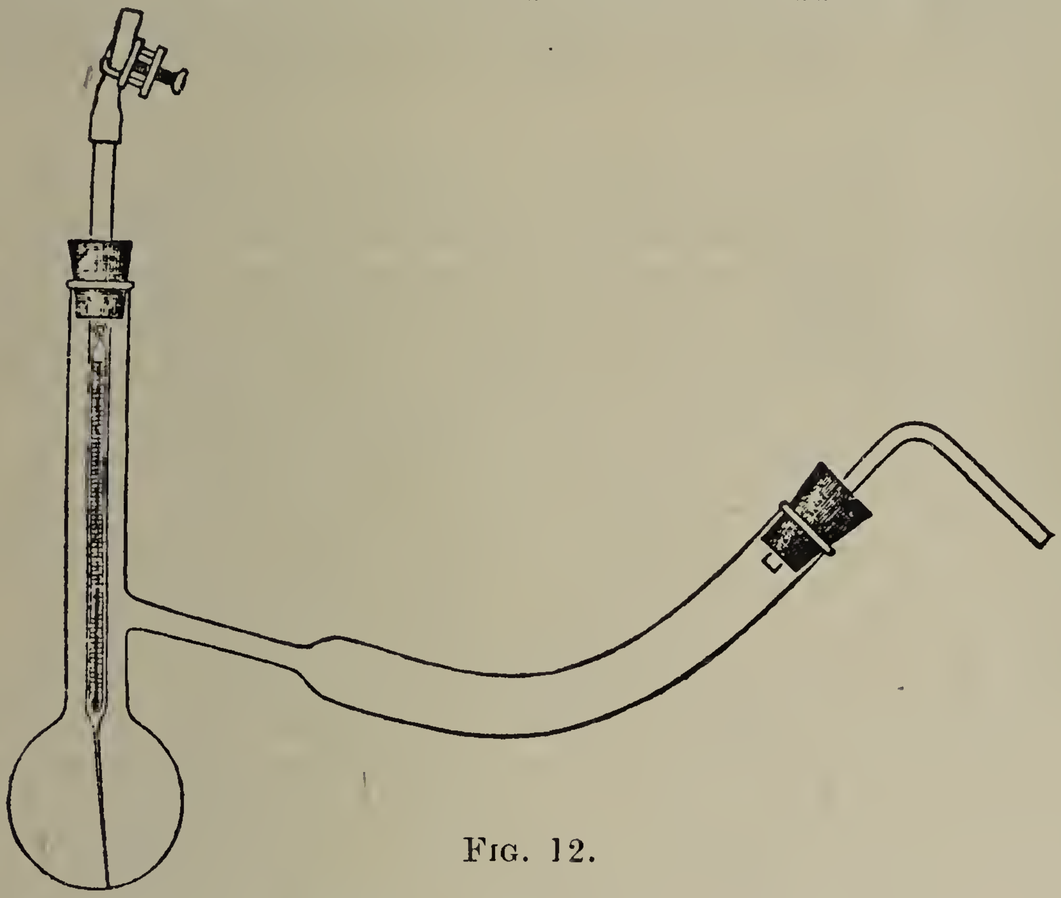


FIG. 12.

*Distillation under Reduced Pressure.**—Attention has already been directed to the great variation in boiling points with variation in temperature. Many carbon derivatives whose decomposition temperature, at the ordinary pressure, is lower than that of their boiling points, can be boiled under reduced pressure at temperatures below the point at which they break down. Distillation under reduced pressure is often the only means of purifying liquids which decompose when boiled at the ordinary pressure, and which cannot be crystallized. This method is of primary importance in scientific research in the laboratory, and is largely used in technical operations.

Distillation under reduced pressure of easily solidifying bodies has been facilitated by the introduction of flasks to which receivers are fused or ground in (Fig. 12). The thermometer is introduced into a thin-walled tube drawn out

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* Compare *Anschütz* and *Reitter*, Die Destillation unter vermindertem Druck im Laboratorium, 2nd ed., 1895, Bonn. The tables in this book record the boiling points of over 400 inorganic and organic substances under reduced pressure. *Georg W. Kahlbaum*, Siedetemperatur und Druck, Leipzig, 1885. Dampfspannkraftsmessungen, Basel, 1893. *Meyer Wildermann*, Die Siedetemperaturen der Körper sind eine Funktion ihrer chemischen Natur (Ber. **23**, 1254, 1468). *W. Nernst* and *A. Hesse*, Siede- und Schmelzpunkte, Braunschweig, 1893. *Lechenberg*, Theorie der gewinnung und Trennung der ätherischen Öle durch Destillation, Leipzig, 1910.

into a capillary, the other end of which is closed with rubber tubing and a clip. For most purposes a two-necked flask (so-called *Claisen* flask) is used. To prevent bumping, air, or, in the case of easily oxidized substances, an inert gas, is drawn through the capillary.

For distillation at very low pressures, a *Gaede* pump (improved by *Volmer*, Ber. **52**, 804) backed by a water pump may be used. This rapidly reduces the pressure to 0·01 to 0·001 mm. See also Anschütz, Ber. **59**, 1791.

A still simpler method of attaining very low pressures consists in the employment of liquid air. A vessel, containing very finely divided pure blood-charcoal, or coconut charcoal, is interposed between the apparatus illustrated in Fig. 12 and the air pump. On cooling it with liquid air the small amount of gas left in the apparatus condenses in the charcoal, and the pressure falls to a fraction of a millimetre. If the apparatus is filled beforehand with CO_2, the charcoal can be omitted (Ber. **38**, 4149).

For distillation under any desired pressure, the apparatus of *Staedel* (Ann. **195**, 218 : Ber. **13**, 839), and *Schumann* (Ber. **18**, 2085), may be used. For mercury thermometers registering temperatures to 550°, see Ber. **26**, 1815 ; to 700°, Ber. **27**, 470.

Fractional Distillation.—Liquids having different boiling points can be separated from mixtures by *fractional distillation*—an operation that is performed in almost every distillation. Portions boiling between definite temperature intervals (from 1–10°, etc.) are collected separately and subjected to repeated distillation, those portions boiling alike being united. To attain a more rapid separation of the rising vapours, these should be passed through a vertical tube, in which the vapours of the higher boiling compound condense and flow back, as in the apparatus employed in the rectification of spirit or benzene. To this end there is placed on the boiling flask a so-called *fractionating column* (*Würtz*). Excellent modifications of this have been described by *Linnemann*, *Le Bel*, *Hempel*, *Young*, and others. For the action of these "heads," see Ann. **224**, 259 : Ber. **18**, R. 101 : Ann. **247**, 3 : Ber. **28**, R. 352, 938 : **29**, R. 187 : **43**, 419 : Chem. Ztg. **37**, 1441. The action of these fractionating columns is increased if enclosed by a highly evacuated jacket (Ber. **39**, 893, footnote).

*Relation of Boiling Point to Constitution.**—(1) Generally the boiling point of members of a homologous series rises with the increasing number of carbon atoms. (2) Among isomeric compounds of equal carbon content, that possessing the more normal structure boils at a higher temperature. The accumulation of methyl groups depresses the boiling point (Chem. News, **100**, 293). It is noteworthy that the lowest boiling isomers possess the greatest specific volume (Ber. **15**, 2571). (3) Unsaturated compounds boil at a higher temperature than those which are saturated. (4) The substitution of a hydrogen atom by a hydroxyl group raises the boiling point about 100°.

The connection existing between the boiling points and chemical constitution of the compounds will be discussed later in the several homologous groups.

5. SOLUBILITY

The hydrocarbons and their halogen substitution products are either insoluble, or only very slightly soluble, in water. They dissolve, however, very readily in alcohol and in ether, in which most other carbon derivatives are also soluble.†

Ether, but slightly miscible with water, is employed to extract many substances from their aqueous solutions, separating funnels being used for this purpose.

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* On the connection between the boiling point and the chemical constitution of a substance, as known at present, see *Graham-Otto*, Lehrbuch der Chemie, Vol I, part 3, p. 535 (1898) ; also *Menschutkin*, C. 1897, II. 1067.

† For the regularities among the solubilities of isomeric carbon derivatives, consult *Carnelley*, Phil. Mag. [6] **13**, 180 ; *Carnelley and Thomson*, J.C.S. **53**, 801.

For apparatus suitable for determining solubility, see *V. Meyer*, Ber. **8**, 998, and *Köhler*, Z. anal. Chem. **18**, 239 ; Ber. **30**, 1752.

Solubilities of organic substances, see *Landolt-Börnstein*, Physik.-chem. Tabellen, 5. Aufl. 1923 : *Seidell*, Solubilities of Inorg. and Org. Substances, **1920** : supplement, 1928 (New York).

The more oxygen a compound contains, the more readily soluble is it in water ; especially is this true when several of the oxygen atoms are present as hydroxyl groups.*

The first members of homologous series of alcohols, aldehydes, ketones, and acids are soluble in water, but as the carbon content increases, the hydrocarbon character, in relation to solubility, becomes more and more evident, and the compounds become more and more insoluble in water.

In addition to water, alcohol, and ether, other liquids are employed as solvents, such as carbon disulphide, chloroform, carbon tetrachloride, methylal, acetone, glacial acetic acid, ethyl acetate, benzene, toluene, xylene, aniline, nitrobenzene, phenol, etc. Light petroleum spirit, derived from American petroleum, is especially valuable ; it is composed of lower paraffins, and is often used to separate compounds from solvents with which it is miscible, because very many organic substances are insoluble or dissolve with difficulty in it.

The solubility of a compound is dependent upon the temperature, and is constant for a definite temperature. This means is frequently employed for purposes of identification.

6. OPTICAL PROPERTIES

(*a*) **Colour.**—The majority of organic compounds are colourless. There are, however, a large number of substances, particularly belonging to the aromatic series, which possess more or less intense colours, and some of which are of very great technical importance as colouring matters. Investigation has shown that there is a correlation between colour and constitution, and that the former depends upon the presence of certain groups in the molecules.† These groups, which are responsible for the colour, are designated as *chromophoric* groups (*O. N. Witt*, Ber. 9, 522). The most important chromophoric groups are the following : $>C:C<$, $>C:O$, $>C:S$, $>C:NH$, $\cdot CH:N\cdot$, $\cdot N(:O):N\cdot$, $\cdot N:N\cdot$, $\cdot N:O$, and $\cdot NO_2$. All chromophoric groups are unsaturated : the development of colour is probably associated with the presence of free partial valencies in such molecules. In this sense, the colour of organic compounds can be said to be due to the presence of " co-ordinately unsaturated " C, N or O atoms. (*Werner* : see later *Pfeiffer*, *Dilthey*.) The introduction of a single chromophore group is unable, with certain exceptions such as $\cdot N:O$ (*Independent chromophores*, Kauffmann) to lead to the development of colour. In general, compounds with a single chromophoric group merely develop an absorption in the ultra-violet (*Hartley*). Aliphatic aldehydes and ketones, for example, show an absorption band between 2800 $\mu\mu$ and 2700 $\mu\mu$. With the introduction of several similar or dissimilar chromophoric groups, the absorption is moved along to the visible part of the spectrum and the compound becomes coloured. The juxtaposition of chromophoric groups in the molecule, with the development of a system of conjugated double bonds, intensifies the unsaturated nature of the compound, and at the same time its colour (Ann. 384, 45), *e.g.* :

$CH_3\cdot CO\cdot CH_2\cdot CO\cdot CH_3$	$CH_3\cdot CO\cdot CO\cdot CH_3$
Colourless.	Coloured (Yellow).

One of the most important combinations of chromophoric groups,

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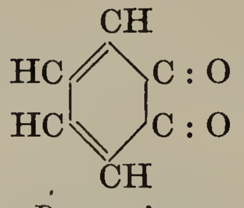
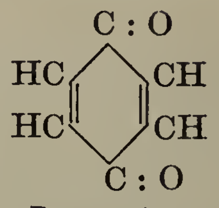
* *Cf.* also *Staudinger*, Anleitung zur organischen qualitativen Analyse (Springer, 1923).

† *H. Ley*, Die Beziehung zwischen Farbe und Konstitution organischer Verbindungen, Leipzig, 1911 : *Henrich*, Theorien der organischen Chemie, Braunschweig, 1924.

which is responsible for many technical colouring matters, occurs in *o*- and *p*-benzoquinones.



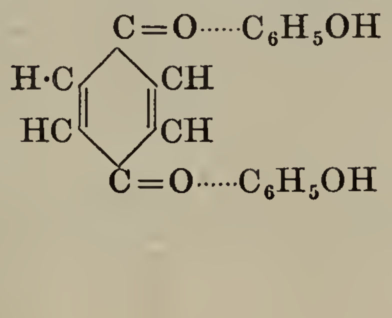
o-Benzoquinone.

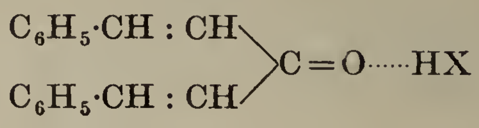


p-Benzoquinone.

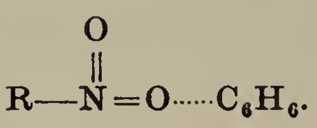
The colour of a compound containing a chromophoric group (such compounds are sometimes described as *chromogens*) is markedly intensified by the introduction of certain substituents such as hydroxyl or amino groups. These groups, which of themselves have no chromophoric properties, are termed *auxochromes* (*cf.* Chem. Ztg. **34,** 1016). Opinions as to the mechanism of auxochromic action are divided (*cf. Kauffmann,* Die Valenzlehre, Stuttgart, 1911). The colouring matters of actual technical importance almost all belong to the aromatic series, and contain in addition to a chromophore, one or more auxochromic groups, which by virtue of their capacity for forming salts facilitate their fixation to animal or vegetable fibres.

The quinhydrones exhibit remarkable colours. These are compounds formed by the union of a quinone with its dihydrogenated reduction product, a dihydric phenol. Quinhydrones invariably display a more marked colour than their related quinones. For example, the simplest quinhydrone, constituted by a molecule of (yellow) benzoquinone and a molecule of (colourless) hydroquinone, forms greenish-black crystals, with a metallic lustre. Quinones yield similar intensively coloured addition products with monohydric phenols, aromatic amines and hydrocarbons (Ann. **368,** 277 : **404,** 1). These compounds are more or less completely dissociated into their components in solution, and are to be regarded as molecular compounds, in which the second molecule is linked to the oxygen atom of the quinone by a co-ordinate link (Ann. **368,** 287 : **404,** 1 : Ber. **46,** 1843). Willstätter in the course of his investigations of Wurster's red (see Vol. II) has shown that the meriquinoid system of the quinhydrones (a benzenoid + a quinonoid nucleus) exists in many colouring matters (Ber. **41,** 1465). The more or less coloured addition compounds of aromatic hydrocarbons, amines and phenols with picric acid, tetranitromethane and similar substances belong to this group. The halochromy of unsaturated ketones, *i.e.* their capacity to combine with acids and salts with the formation of deeply coloured labile, salt-like addition products should also be mentioned here (*cf. P. Pfeiffer,* Ann. **376,** 285 : **383,** 92 : **404,** 1 : **412,** 53). The quinones, as a special class of unsaturated ketones, show the same property. The similarity of the various types of addition compound is demonstrated by the following formulæ :





$$(C_6H_5{\cdot}CH:CH)_2C{=}O\cdots HX$$



$$R{-}\overset{\overset{\displaystyle O}{\|}}{N}{=}O\cdots C_6H_6.$$

As an explanation of the intense colour of these molecular compounds, it may be considered that through the partial saturation of an oxygen valency by the addendum, free valencies are formed on the carbon atom of the carbonyl group, or nitrogen atom of the nitro group, and thereby develop in these atoms the character of a strong chromophoric group (Ann. **376**, 292 : **383**, 92 : **404**, 1). The compounds are thereby represented similarly to the intensively coloured triarylmethyls, $Ar_3C\cdots$ (Ann. **371**, 1) and the metallic derivatives of the ketones, the so-called metal ketyls, $R_2\underset{\vdots}{C}\cdot OM$ (Ber. **46**, 2840).

Compounds of the type of triphenylcarbinol, $(C_6H_5)_3C\cdot OH$, show particularly well-marked halochromy. It is probable that here, too, the development of colour is due to the formation of free partial valencies (Ann. **383**, 121 : *cf.* Ber. **38**, 570 : **39**, 2977, and under halochromy, p. 53).

According to Dilthey (J. pr. Chem. **109**, 237) the development of an ionic link is of great importance as regards the colour of an organic compound. Phenyltolylnaphthylchloromethane is colourless, and dissolves in cold benzene to form a colourless solution. On warming its solution in tetrachloroethane, acetic anhydride, etc., an intense violet colour is produced, due to the dissociation of the chlorine and the formation of an unsaturated central atom (chromophore) as follows :

$$\underset{\text{Colourless.}}{(C_6H_5)(C_7H_7)(C_{10}H_7)CCl} \rightleftarrows \underset{\text{Coloured.}}{[(C_6H_5)(C_7H_7)(C_{10}H_7)C]^+\ [Cl]^-}$$

The regularities in the colours of the salts of the di- and triphenylmethane dyestuffs, the indigoid colouring matters, etc., can be viewed from the same standpoint : " co-ordinatively unsaturated " nitrogen atoms can be regarded as the cause of the deep colour, and the same holds for the oxazine, thiazine and azine colouring matters (J. pr. Chem. **109**, 298 : Z. angew. Chem. **1926**, 546 : **1927**, 939).

For the practical study of the absorption by compounds containing chromophores, the method of graphic representation introduced by Hartley and developed by Baly, Bielecki, Henry, Weigert and others is of value. Ordinates are the thickness of the layer in millimetres, or for practical reasons, the logarithm of the thickness, for a solution of suitable concentration, the abscissæ the frequencies (or sometimes wave-lengths).

The following absorption curve of azobenzene is taken from Ber. **43**, 1189 : The curve shows that red azobenzene shows two well-marked absorption maxima : the strongest at *a*, frequency 3200, and clearly shown by a *N*/10000 solution, the weaker at *b*, frequency 2200, and only shown by stronger solutions. Similar absorption curves are useful in showing constitutional differences, especially if one measures the absorption quantitatively as done by Bielecki and Henry (Ber. **45**, 2819 : **46**, 1304, 2596, 3627, 3650 : see also the numerous absorption curves in *Landolt-Börnstein*, Physikal.-chem. Tabellen, Ergänzungsbd. 1927, 437).

The theory of light absorption has been developed by Lambert. According to him it can be represented by the following equation :

$$I = I_0 . e^{-Kd}$$

where I_0 is the intensity of the incident light, and I the intensity of the emergent light, *d* the thickness, K a constant for the compound concerned, and *e* the basis of natural logarithms (2·71828...). The equation can be rewritten :

$$\ln \frac{I_0}{I} = K.d \text{ or } \log \frac{I_0}{I} = k.d$$

(where $k = K/2{\cdot}3026$ to convert to decimal logarithms).

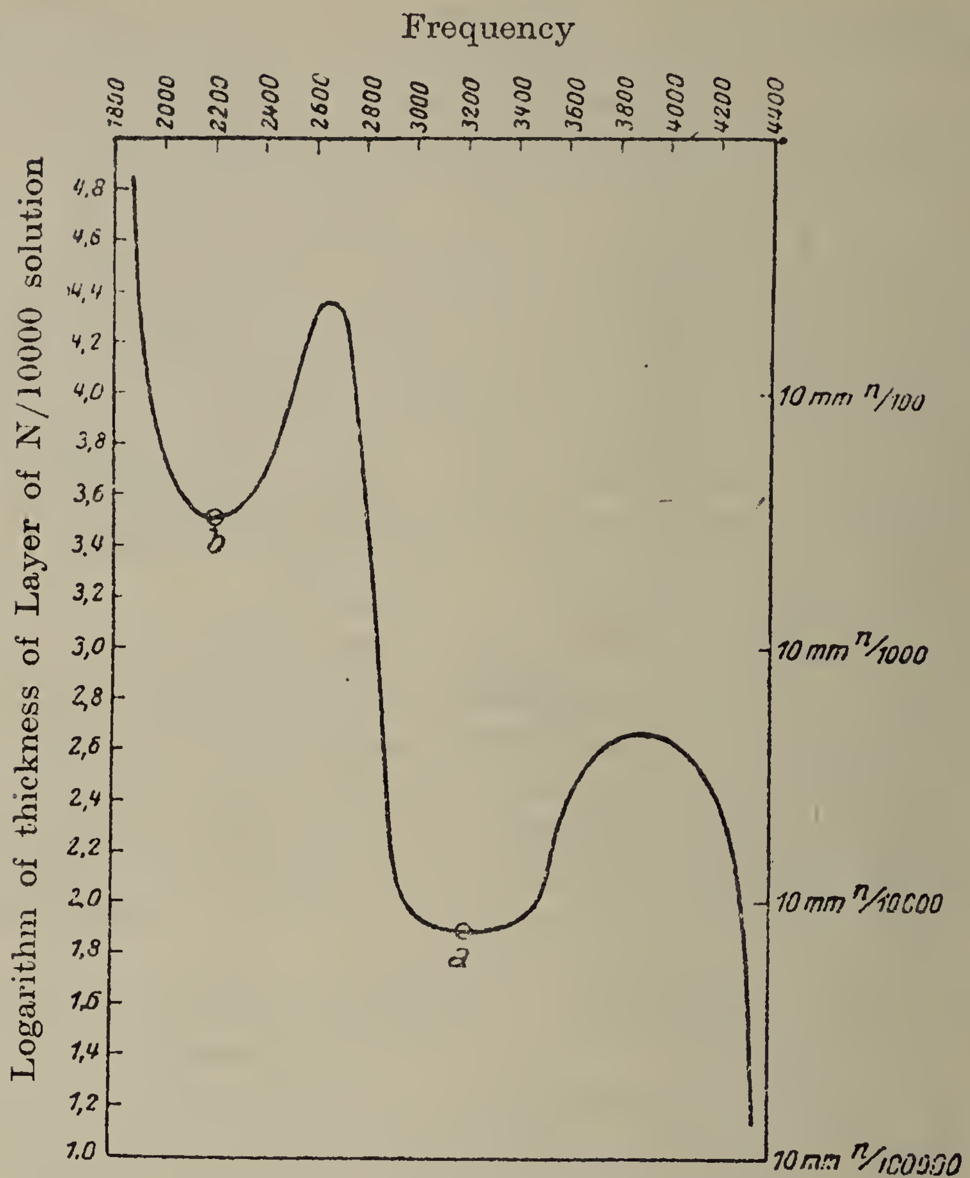


FIG. 13.

The expression $\log \frac{I_0}{I} = k.d$ is described as the extinction. In the case of solutions the concentration is introduced

$$\text{Extinction} = \epsilon = \log \frac{I_0}{I} = k.c.d.$$

From this formula, *Beer's law* is deducible, which says that for equal absorption (ϵ equal) the concentration is inversely to the thickness of the absorbing layer:

$$c_1 : c_2 : : d_2 : d_1.$$

This law is the basis of colorimetry.

Fluorescence.—The fluorescence of organic compounds is determined by the presence of various fluorophoric groups in the molecule (*R. Meyer*, Ber. **31**, 510: C. 1900, II. 308: Chem. Ztg. **29**, 1027: Ann. **344**, 30: Ber. **41**, 2988, 4396: Z. physik. Chem. **86**, 36: *H. Kauffmann*, Die Beziehung zwischen Fluorescenz und chemischer Konstitution, Stuttgart, 1906: Ann. **393**, 1: Ber. **54**, 2492: **55**, 3911).

(*b*) **Refraction.***—The carbon compounds (like all transparent substances) possess the power of refracting light to a varying degree.

The *refractive index* (*n*) for homogeneous light passing from medium

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* *F. Eisenlohr*, Spektrochemie organischer Verbindungen, Stuttgart, 1912, *W. A. Roth* and *F. Eisenlohr*, Refraktometrisches Hilfsbuch, Leipzig, 1911.

1 into medium 2, represents the ratio of the velocities of propagation v_1 and v_2 in both media; $n = \frac{v_1}{v_2}$. For single refracting media, in which similar optical behaviour is observed in all directions (a condition which is seldom found in crystals), n is independent of the direction of the incident light, so that if i and r are the incident and refractive angles $n = \frac{v_1}{v_2} = \frac{\sin i}{\sin r}$, a constant for light of a definite wave-length.

In the determination of refractive indices, in order to obtain readily reproducible results, monochromatic light of known wave-length is used. The wave-lengths usually employed are sodium light (D line) and the three principal hydrogen lines H_α (red), H_β (green) and H_γ (violet). The refractive index varies with temperature, and this must also be recorded: n_D^{20}, for example, indicates the refractive index for sodium light at 20° C. The values so determined are affected by dispersion, and it is not at present possible to calculate a refractive index to eliminate the dispersion effect by any dispersion formula.

The determination of refractive index can be carried out very rapidly, with a small quantity of liquid, by the use of the Abbe or Pulfrich refractometers, or a Zeiss refractometer (Z. physik. Chem. **18,** 294: Ber. **24,** 286).

Specific Refractive Power.—The refractive index (n) varies with the temperature, consequently also with the specific gravity of the liquid.

Their relation to each other is approximately expressed by the equation:

$$\frac{n-1}{d} = \text{const.} \qquad \text{or} \qquad \frac{n^2-1}{n^2+2} \cdot \frac{1}{d} = \text{const.}^*$$

(Gladstone's formula). n-formula. (Lorenz and Lorentz's formula). n^2-formula.

where d is the sp. gr. of the liquid, determined at the same temperature as the refractive index. The constant remains practically unchanged for any temperature.

Molecular Refractive Power or Molecular Refraction is the specific refractive power of a substance multiplied by its molecular weight M. It is represented by $[R_G]$ or $[R_L]$, according to whether Gladstone's or the n^2-formula is adopted:

$$[R_G] = \frac{n-1}{d} . M. \qquad [R_L] = \frac{n^2-1}{n^2+2} \cdot \frac{1}{d} \cdot M.$$

It is immaterial which of the two formulæ is employed in the examination of stoichiometrical questions, so long as liquid substances are referred to.

The Gladstone formula gives values which fall with rise in temperature, whereas with the Lorenz-Lorentz formula, values tend to rise. At the present day the n^2-formula is used almost exclusively.

The molecular refraction of a liquid carbon compound is equal to the sum of the atomic refractions r, r', r'':

$$[R] = ar + br' + cr'',$$

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* *Graham-Otto,* Ausführliches Lehrbuch der Chemie, Bd. I, 3 Abt., p. 567 (1898): *H. A. Lorentz,* The Theory of Electrons, Leipzig, 1909: *Eucken,* Grundriss der physikalischen Chemie, Leipzig, 1922.

in which *a*, *b*, *c*, represent the number of elementary atoms in the compound. The atomic refractions of the elements are deduced from the molecular refractions of the compounds obtained empirically, in the same manner as the atomic volumes are obtained from the molecular volumes. Only the univalent elements have a constant atomic refraction ; that of the polyvalent elements, *e.g.* oxygen, sulphur, carbon, is influenced by their manner of union.

This is seen in the rise in the molecular refraction by a constant quantity, amounting to 1·733 in the case of the n^2-formula, for each double bond. A treble bond possesses the n^2 value of approximately 2·398 : these values are referred to as "*increments*."

The following table gives the atomic refractions for various atoms calculated from numerous observations by Eisenlohr (Z. physik. Chem. **75**, 585 : **83**, 429) :

		H_α.	D.	H_β.	H_γ.
Carbon (single bond)	C	2·413	2·418	2·439	2·466
Hydrogen	H	1·092	1·100	1·115	1·122
Oxygen (carbonyl)	O''	2·189	2·211	2·247	2·267
Oxygen (ether)	$O<$	1·639	1·643	1·649	1·662
Oxygen (hydroxyl).	O'	1·522	1·525	1·531	1·541
Chlorine	Cl	5·933	5·967	6·043	6·101
Bromine	Br	8·803	8·865	8·999	9·152
Iodine	I	13·757	13·900	14·224	14·251
Double bond		1·683	1·733	1·824	1·893
Triple bond		2·328	2·398	2·506	2·538

The atomic refractions of sulphur and nitrogen vary enormously according to the mode of linkage of these elements (Z. physik. Chem. **79**, 129, 481 : Ann. Chim. et Phys. [8] **25**, 529 : J.C.S. **101**, 1259). Chlorine shows a higher refractivity in acid chlorides than in alkyl chlorides (Ber. **45**, 2781).

The molecular refraction calculated from the observed density and refractive index can be compared with that calculated by addition from the various atomic refractions given in the above table. By this method important evidence as to the mode of linkage of the atoms in an organic compound can be obtained. Thus, for example, the molecular refraction of benzene which is 5·2 (3 × 1·733) units higher than that calculated for $C_6 + H_6$ lends support to the existence of three double bonds in the benzene nucleus.

In many tautomeric (desmotropic) compounds (see p. 48) the determination of the molecular refraction enables a decision to be arrived at as to whether the enol- or keto-form is being dealt with, or the proportions of each when they exist together (J. pr. Chem. [2], **50**, 119 : Ber. **38**, 1868 : **44**, 3514).

More recent investigations of Brühl (Ber. **40**, 878, 1173 : **41**, 3712) and of v. Auwers and Eisenlohr (J. pr. Chem. [2] **82**, 65 : **84**, 1, 37 : Ann. **387**, 165, etc.) have shown that even more subtle structural differences in the molecule influence the molecular refraction. For example, compounds with systems of conjugated double bonds (p. 28) almost invariably show a higher molecular refraction than that calculated from the above table, even when allowance has been made for the existence of the double bonds in the calculation. This excess in the molecular refraction over that calculated is designated by Brühl the *exaltation.* This value, unlike the increment due to isolated double bonds, is not a constant quantity, but increases with increase in the molecular weight of the compound. To obtain comparable values for the exaltation, a device of v. Auwers and Eisenlohr is used, the observed exaltation being divided by the molecular weight and multiplied by 100. The value so found is designated the specific exaltation and is denoted by the symbol $E\Sigma_r$, the actually observed exaltation being denoted by EM_r (Ber. **43**, 806).

Another value frequently used in attacking constitutional problems is the *molecular dispersion.* This is the difference between the molecular refractions for light of two different wave-lengths. In practice hydrogen light is usually used and the lines H_α and H_γ used. The molecular dispersion is then given by the formula

$$[R_L]_{H_\gamma} - [R_L]_{H_\alpha} = \left(\frac{n_\gamma^2 - 1}{n_\gamma^2 + 2} - \frac{n_\alpha^2 - 1}{n_\alpha^2 + 2}\right)\frac{M}{d}.$$

Here also the observed values can be compared with the calculated. If the observed value exceeds the calculated, the term *dispersion exaltation* is used, and where less than calculated the term *depression.* For comparative purposes, the actually observed dispersion is not usually used, but the observed dispersion expressed as a percentage of the calculated (Ber. **43**, 806).

The development of exaltation is connected intimately with the constitution of the compound concerned as shown by the investigations in particular of v. Auwers and Eisenlohr (Ber. **43**, 806, 827 : J. pr. Chem. [2] **82**, 65 : **84**, 1 : Ann. **387**, 165 : **409**, 149 : **410**, 287 : **413**, 253 : **415**, 98, 169).

If both refraction and dispersion show exaltations, the compound has either

(*a*) a semicyclic double bond,
(*b*) a *cyclo*propane or *cyclo*butane ring,
(*c*) an undisturbed conjugated double bond.

At times, however, the findings are disturbed by the accumulation of substituent groups.

Ring closure of olefinic compounds (dienes and trienes) to ring compounds is always associated with a diminution of the specific exaltation (Ann. **415**, 98).

(*c*) **Dielectric Constant.**—The electrostatic force by which two electrified bodies affect one another varies with the nature of the insulating "dielectric medium" which separates them. Taking air as unity, the measurement made with another substance under similar circumstances gives the *dielectric constant* of that medium. This value, usually indicated by ε, has been taken for a large number of carbon compounds ; * for example

	ε		ε
Gases and vapours, about	1·0	Fatty acids, about	2·6–7·0
Liquid hydrocarbons	2·0–2·5	Fatty acid esters	5–9
Carbon disulphide	2·6	Fatty alcohols	16–35
Ethyl ether	4·5	Water	80

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* On the method of measurement for chemical purposes, see *Nernst,* Z. physik. Chem. **14**, 622 : **24**, 21 : Wied. Ann. **57**, 215 : **60**, 600 : *Drude,* Z. physik. Chem. **23**, 267.

The electromagnetic theory of light is based on the fundamental principle that light and electromagnetic waves are of the same nature, differing from one another only in length. The refractive index for an infinitely long wave can be closely connected to the dielectric constant, by the relation $\sqrt{\varepsilon} = n\alpha$. The determination of the dielectric constant thus supplies directly a value for the refractive index free from dispersion, analogous to the Lorenz formula (p. 65).

$$M \cdot \frac{\varepsilon - 1}{\varepsilon + 2} \cdot \frac{1}{d} = \text{const.}^*$$

The values obtained in investigations so far carried out have not led in general to a good correspondence with those derived by optical methods, whilst the optical molecular refraction measurements show an additive character (at least for compounds of similar constitution), the values obtained by electrical methods are influenced by insignificant differences in constitution of each substance (C. 1911, I. 953). In this case there is no possibility of calculating "atomic refractions," but rather to trace and disclose differences in constitution by electrical means, for which purpose it is of great assistance. Under certain circumstances the attendant phenomenon of *anomalous electrical absorption* is to be observed, *i.e.* the partial change of electrical into heat energy. Almost all the non-conducting carbon compounds which give rise to this absorption contain the hydroxyl group. On this observation is based a method of detecting and demonstrating the mutual change of keto- and enol- forms (*Drude*, Ber. **30**, 940; Z. physik. Chem. **23**, 308, 318). Further progress in this investigation will doubtless yield important results.

The vapours of many groups of aliphatic and specially aromatic bodies absorb *Tesla currents* at ordinary pressure and change them into light waves. Such substances, for example, are the primary aromatic amines, and the simple aliphatic aldehydes and ketones. In the latter case the keto- group seems to be the vehicle of the luminescence, at any rate neither the vapours of paraldehyde nor of acetaldehyde become illuminated (*H. Kauffmann*, Ber. **35**, 473).

(*d*) **Optical Rotatory Power.**† *Rotation of the Plane of Polarization by Liquid or Dissolved Carbon Compounds.*—Biot, in 1815, observed that many naturally occurring bodies such as the sugars, the terpenes, and camphors, were capable of rotating the plane of polarized light. He also showed, in 1817, how the vapours of turpentine also deviated the plane of polarization, and concluded that this power was a property of chemical molecules. Such bodies are termed *optically active compounds*.

Specific Rotatory Power [α].—The angle of rotation α is proportional to the length l of the rotating column (usually expressed in decimetres); hence the expression $\frac{\alpha}{l}$ is a constant quantity. To compare substances of different density, in which very unequal masses may be contained in this column, they must be referred to a like density, and hence the rotation must be divided by the sp. gr. of the substance at a definite temperature. The expression

$$[\alpha] = \frac{\alpha}{l.d}$$

is called the *specific rotatory power* and is designated by $[\alpha]_D$ when the rotation is referred to the yellow sodium line D. For solid,

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* *Landolt* and *Jahn*, Z. physik. Chem. **10**, 289. See also *Graham-Otto*, Lehrb. der Chemie, I. part 3, p. 650, 1888.

† *Landolt*, Das optische Drehungsverm gen organischer Substanzen und die practische Andwendung derselben, 2nd edition, Braunschweig, 1898. *Walden*, Ueber das Drehungsvermögen optisch aktiver Körper, Ber. **38**, 345.

active substances, in an indifferent solvent, the equation employed is

$$[\alpha] = \frac{100\alpha}{p.l.d}, \quad \text{or} \quad [\alpha] = \frac{100\alpha}{l.c}$$

where p represents the quantity of substance in 100 parts by weight of the solution, c the weight of substance in 100 c.c., and d represents the specific gravity of the latter.

This specific rotatory power is constant for every substance at a definite temperature; it varies, however, with the latter, and, in the case of solutions, with the nature and quantity of the solvent. So much is this the case, that under various conditions the angle of rotation for one and the same substance can become zero or even change in sign. Therefore, in the statement of the specific rotatory power of dissolved substances the temperature and percentage strength of the solution are always given as well as the nature of the solvent.

In many cases the addition of substances such as salts, etc., causes a change in the rotation. Such active bodies, including tartaric acid, malic acid, mandelic acid, and others, which contain an alcoholic hydroxyl group, are powerfully influenced by the addition of alkali borates, molybdates, tungstates, and uranates. The phenomenon depends apparently on the formation of complex combinations (Ber. **38**, 3874, etc.), and can sometimes be used to increase the rotation of active substances, of which the rotatory power would otherwise be too small to be measured alone, either on account of specific value being insignificant or because the solution employed is too weak. (See *Landolt*, *loc. cit.* p. 220: *Walden*, Ber. **30**, 2889.)

Mutarotation is the term used to denote the phenomenon first observed by Dubrunfaut in 1846 of an alteration of the initially observed rotation of a compound. The rapidity with which a solution reaches its constant end-value is markedly influenced by the H- and OH-ion concentration of the solution. The phenomenon depends upon an isomeric change taking place in the solute.

Numerous investigations have been made in studying the relation between constitution and the magnitude of the optical rotatory power (*Walden*, Lecture, Ber. **38**, 355: *Rupe*, Ann. **327** to Ann. **409**). The action on polarized light appears to be conditioned by the same constitutional influences as those affecting the molecular refraction.

In the case of compounds containing several asymmetric carbon atoms, particularly the sugars, the investigations of C. S. Hudson have produced methods by which the contribution of the various individual asymmetric atoms can be calculated, and from this the specific rotatory power of compounds for which it is unknown, can be prophesied (J.A.C.S. **32**, 338: **33**, 405: **39**, 462 (phenylhydrazides): **40**, 813: **41**, 1141 (amides of sugar acids).

Molecular rotatory power is the product of the specific rotatory power $[\alpha]$ and the molecular weight M, for convenience to avoid very large figures, divided by 100. It is represented by $[M]$ or $M[\alpha]$

$$[M] \text{ or } M[\alpha] = \frac{[\alpha]}{100} \times M.$$

The most convenient apparatus for the measurement of optical rotation are described in the monograph of Landolt previously referred to (footnote, p. 68) or in *Houben*, Arbeitsmethoden, Bd. I, p. 848 (1921). Apparatus for the use of small quantities of liquid, see Monatsh. **29**, 333: Ber. **44**, 129.

In 1848 Pasteur demonstrated that in optically active substances, such as tartaric acid and its salts, the rotatory power is intimately connected with the crystalline form, and is usually connected with the presence of hemihedral faces. Pasteur considered the asymmetric structure of the molecules of optically active carbon compounds to be the cause of their remarkable action upon polarized light.

According to the theory of van 't Hoff and Le Bel, the activity of the carbon compounds is dependent upon the presence of *asymmetric carbon atoms* or on the asymmetric arrangement of atoms attached to a carbon skeleton in space (p. 38).

Most optically active carbon compounds contain one or more asymmetric carbon atoms: compounds are, however, known whose optical activity is due to asymmetric nitrogen or other atoms. However, there are many compounds containing such atoms, which, when they exist as liquids, or when in solution, have no effect upon polarized light. This is true when two molecules of opposite but equal rotatory power unite to form a molecule of a physical, polymeric compound, *e.g.* inactive lactic acid, inactive malic acid, inactive asparagine, inactive aspartic acid, racemic acid, etc.; also, when the half of a molecule neutralizes the rotation produced by the other half, as in *meso*tartaric acid.

It has also been shown that in the conversion of optically active bodies into their derivatives the activity continues so long as the latter contain asymmetric carbon atoms; when the asymmetry disappears, the derivatives become inactive. The two active tartaric acids yield two active malic acids; active asparagine yields active aspartic acid, active malic acid, etc., whilst the symmetrical succinic acid that is obtained by further reduction is inactive.

By the transposition of two substituents on an asymmetric carbon atom it is theoretically possible to reverse the optical activity of a substance, and this has been carried out practically in the case of *iso*propylmalonamic acid, the *d*-acid being converted into its enantiomorph by a series of reactions by which the COOH and $CONH_2$ groups were interchanged (Ber. **47**, 3181).

If different groups containing asymmetric carbon atoms are introduced into a molecule, their optical activities are cumulative and the resultant rotation is the sum of the individual rotations (*Guye*, Compt. rend. **119**, 953: **120**, 632: **121**, 827: **122**, 932: *Walden*, Z. physik. Chem. **17**, 721: *cf.* however, *Rosanoff*, Z. physik. Chem. **56**, 565).

By changes in one of the substituent groups on an asymmetric carbon atom, as for example by introduction of an ethylenic linkage or ring-formation or change of an alkyl group (Compt. rend. **136**, 1222: **140**, 1205: J.C.S. **99**, 218: **105**, 2226: Ann. **402**, 149) or by alkylation or acylation of NH- or OH-groups (Ber. **34**, 2420: J.C.S. **87**, 864) the rotatory power is frequently greatly altered. A general relation between the magnitude of the rotation and the nature of the groups attached to an asymmetric carbon atom has not yet been evolved.

*Walden Inversion.**—In certain cases it is possible by a series of reactions to change one optically active substance into its mirror image. For instance, ethyl (—)-malate† yields with PCl_5 ethyl (+)-chlorosuccinate: (+)-chlorosuccinic acid with silver oxide yields (+)-malic acid. By a similar series of reactions, ethyl (+)-malate can be made to yield (—)-malic acid. If, however, the replacement of the halogen is carried out by potassium hydroxide instead of silver oxide, reversal of rotation occurs and (+)-chlorosuccinic acid yields (—)-malic acid. These relationships are expressed in the following diagram:

$$\begin{tikzcd}
\text{(−)-Malic acid} \arrow[d, shift right, "PCl_5"'] & \text{(−)-Chlorosuccinic acid} \arrow[l, "Ag_2O"'] \arrow[d, shift right, "KOH"'] \\
\text{(+)-Chlorosuccinic acid} \arrow[u, shift right, "KOH"'] \arrow[r, "Ag_2O"] & \text{(+)-Malic acid} \arrow[u, shift right, "PCl_5"']
\end{tikzcd}$$

This transformation was first discovered and investigated by P. Walden (Ber. **29**, 132: **32**, 1833, 1855) and is therefore known as

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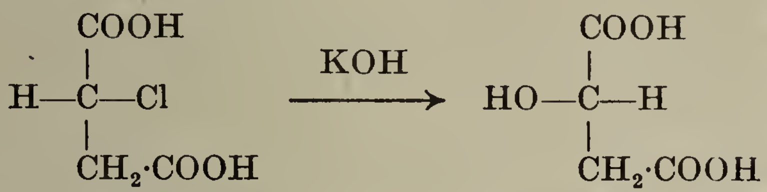
* *P. Walden*, Optische Umkehrerscheinungen (Waldensche Umkehrung) Vieweg, Braunschweig, 1919.

† The signs (+) and (—) denote the actual direction of optical rotation of the compound.

the *Walden Inversion.* Other examples of the transformation of optical antipodes have been investigated more recently, such as the conversion of optically active α-aminoacids into the α-halogen fatty acids by E. Fischer and his co-workers (Ber. **45**, 2447 : see also McKenzie, Clough *et al.*, J.C.S. **93**, 811 : **97**, 121 : **103**, 687 : Frankland and Garner, J.C.S. **105**, 1101).

It must be understood that a mere alteration of the direction of rotation as a result of a chemical reaction is in no sense evidence that a Walden inversion has occurred, and it cannot therefore be decided, without further information, at which stage in the above cycle the actual inversion occurs.*

The stereochemical significance of the Walden inversion is that two groups attached to the asymmetric carbon atom have exchanged places. We can assume, for example, that the inversion occurs in the reaction between potassium hydroxide and chlorosuccinic acid, whereby the entering OH group does not occupy the same position as the halogen atom it has displaced. This can be represented by projection formulæ as follows :



$$\begin{array}{c} \text{COOH} \\ | \\ \text{H—C—Cl} \\ | \\ \text{CH}_2\cdot\text{COOH} \end{array} \xrightarrow{\text{KOH}} \begin{array}{c} \text{COOH} \\ | \\ \text{HO—C—H} \\ | \\ \text{CH}_2\cdot\text{COOH} \end{array}$$

There occurs, therefore, in the Walden inversion an anomalous substitution and it has been attempted to explain it by the assumption that there is a primary addition product of the reacting substances, which then breaks down to yield the final products (Ann. **381**, 123 : **386**, 65, 374) : the occurrence of this reaction is, however, irregular, and cannot be influenced experimentally. Emil Fischer summarizes the Walden inversion as follows : " If substitution occurs at an asymmetric carbon atom, we do not know to which stereochemical series the product will belong " (*cf.* also *Walden*, Lecture, Ber. **58**, 237).

Asymmetric compounds synthesized from inactive compounds are inactive. This is because the two optical antipodes have the same energy content and are each equally likely to be formed in a chemical reaction. A so-called " *asymmetric synthesis*," *i.e.* the formation of an optically active substance from an inactive without intermediate formation of a racemic compound has been carried out, but hitherto only with the assistance of another active compound or an enzyme. For example, an active mandelonitrile is obtained from benzaldehyde and hydrogen cyanide under the catalytic action of quinine or quinidine (Biochem. Z. **46**, 7 : see also Ber. **37**, 1368 : **41**, 752 : Z. physik. Chem. **73**, 25 : J.C.S. **95**, 544). As regards the formation of active substances in living organisms, there is at present no explanation of the initial production of an optically active substance in plants (*cf.* Ber. **42**, 141 : Biochem. Z. **52**, 439 : Ber. **53**, 119).

Racemic Bodies.—The typical substance, racemic acid, has given its name to all similar inactive mixtures of the two optical antipodes. The racemic substance differs from its components also in that it forms crystals which do not give rise to enantiomorphic modifications. The density of the racemic body is

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* Explanation of this cycle, see Ber. **61**, 509.

generally, but not invariably, greater and its solubility less than the corresponding active substances, similarly there is no general rule for the relative position of the melting point.

When the crystalline form of an inactive substance cannot be observed with accuracy, as often happens, and when at the same time, the melting point lies lower than that of either of the optically active components, then doubt may arise whether it is a true racemate or a mixture of equal quantities of the optical antipodes. A variety of tests can be applied. The melting point may be taken after a small quantity of one of the active components has been added to the inactive substance. The composition may be determined, as well as the optical behaviour, of a saturated solution of the inactive body as compared with that of a mixture of the inactive and one active substance. If the addition of the active body causes a lowering of the melting point of the inactive substance, a change in the concentration and in the optical activity of the saturated solution, then the substance is a racemic one; if, on the other hand, the melting point rises, and the concentration and inactivity of the solution are unaltered, then the inactive body is a mixture.

The formation of a racemic substance is dependent on the temperature. Above or below its *transition temperature* the body may be a racemic body or an enantiomorphic mixture. The results of the above experiments hold good, then, only for the particular temperature at which they are carried out, and a series of experiments over a wide range of temperature is necessary to obtain a complete insight into the matter.

These practical tests are, in part, the direct result of the considerations on heterogeneous equilibria as put forward in Gibb's *phase rule* (*van 't Hoff*, Ber. **31**, 528: *Ladenburg*, Ber. **32**, 1822: *Roozeboom*, Z. physik. Chem. **28**, 494, etc. Also Ber. **33**, 1082).

Pseudo-racemic mixed crystals, although inactive, possess the form of the active modifications, without, however, the hemihedric faces (J.C.S. **71**, 889: **75**, 42).

Resolution of Inactive Carbon Compounds into their Optically Active Components

The synthesis of optically active carbon compounds is easily realized by direct methods, because it is possible to separate the *dextro-* and *lævo*-rotatory components in an inactive molecule. The following methods, 1, 2, and 5, were employed by Pasteur (1848) in his study of the racemates and racemic acid. This classic investigation supplies the firm experimental basis for the theory of *stereochemistry* or the space chemistry of carbon (p. 36).

Method 1, *based upon resolution by crystallization.*—The substance itself, or its derivatives with optically inactive compounds, is crystallized at varying temperatures and from various solvents. In the case under consideration it is possible to separate two substances showing enantiomorphous hemihedrism by actually picking out those crystals exhibiting the particular forms. Thus, from a solution of sodium ammonium racemate below 28° hemihedral crystals of sodium ammonium *dextro-* and *lævo*-tartrates can be obtained (Ber. **19**, 2148).

Method 2, *dependent upon the formation of compounds with optically active substances.*—Pasteur succeeded in separating *d*- and *l*-tartaric acids through their quinicine and cinchonine salts. This was because these, being no longer enantiomorphous, were distinguished by their varying solubility, and so could be very easily separated from each other.

Ladenburg first used the latter method to resolve *inactive bases* by forming salts of the latter with an active acid. It was thus that he decomposed synthetic inactive coniine (α-*n*-propylpiperidine) by means of *d*-tartaric acid into its active components, and completed the synthesis of the first optically active vegetable alkaloid—coniine—which occurs in hemlock (*q.v.*).

Camphorsulphonic acid and chloro- and bromocamphorsulphonic acids are of great value for this purpose.

The resolution of symmetrical dimethylsuccinic acid by the use of active triethylenediaminecobalti-compounds is worthy of mention (Ber. **46**, 3229).

The resolution of racemic substances is not always immediately effected by their combination with optically active compounds: sometimes the optically active substance combines with the racemic substance to form a semi-racemic compound which only decomposes into the two active components at a particular temperature (*Ladenburg*, Ber. **31**, 1969 : **32**, 50).

Method 3, *based on the formation of esters or amides* between racemic and optically active substances.—Racemic mandelic acid can be partially turned into the *l*-menthol ester, whereby the residue consists of an excess of *l*-mandelic acid. If *l*-quinic acid be heated with *rac.* α-phenylethylamine, the *dextro-rotatory* acid, which does not take part in the amide formations, remains behind (Ber. 38, 801).

Method 4.—Enzymes, such as maltase or emulsin, decompose racemic glucosides by hydrolysing one component (*E. Fischer*, Ber. **28**, 1429).

Method 5.—On introducing some suitable fungus such as *Penicillium glaucum* into an aqueous solution of an inactive mixture, capable of resolution, one modification of the mixture will be destroyed during the life-process of the fungus ; thus racemic acid yields *l*-tartaric acid, *inactive* amyl alcohol yields *d*-amyl alcohol, *dl*-methylpropylcarbinol yields *l*-methylpropylcarbinol, *dl*-propylene glycol yields *l*-propylene glycol, etc.

One fungus may leave an optical modification untouched which another may destroy. *Penicillium glaucum* or *Bacterium termo* will leave *d*-mandelic acid from the synthetic inactive racemic acid, whilst *Saccharomyces ellipsoideus* or *Schizomycetes* leave the *l*-acid untouched. For the literature of the resolution of racemic compounds, see *Landolt*, Optisches Drehungsvermögen, etc., 2nd edition, p. 86, 1898.

Carbon compounds, in which an asymmetric atom is not present, cannot be decomposed by these methods (Ann. **239**, 164 : Ber. **18**, 1394).

Similar methods enable the resolution of racemic compounds containing asymmetric nitrogen, phosphorus, sulphur, etc., atoms to be effected.

Conversion of Optically Active Substances into their Optically Inactive Modifications

Whilst soluble salts of optically inactive, resolvable carbon compounds may be resolved by crystallization under proper conditions of temperature, many others reunite to form a salt of the inactive body, especially if the latter dissolves with difficulty. Solutions of calcium *lævo-* and *dextro*-tartrates when mixed yield a precipitate of calcium *dl*-tartrate, which dissolves with difficulty. The free, optically active modifications unite, as a rule, very easily when mixed in solution, to form the inactive decomposable modification, *e.g.* *l*- and *d*-tartaric acid yield racemic acid. The esters of these acids behave in a similar manner : *l*- and *d*-tartaric methyl esters unite directly and in solution to form racemic methyl ester (Ber. **18,** 1397). Also, in energetic reactions, or when heated, the active varieties rapidly pass into the inactive forms, *e.g.* *d*-tartaric at 175° yields racemic acid, and at 165° *meso*tartaric acid. At 180° *d*- and *l*-mandelic acids pass into inactive mandelic acid. Some optically active halogen substitution products of carboxylic acids undergo auto-racemization, even at ordinary temperatures (Ber. **31,** 1416).

Compounds containing the grouping $\begin{matrix}R\\R'\end{matrix}\!\!>\!CH{\cdot}CO{\cdot}$ are particularly easily racemized under the action of alkaline reagents, the phenomenon being referred to the tendency of compounds of this type to pass into a tautomeric form (Ann. **373,** 92 : Ber. **47,** 843).

A corresponding behaviour is observed in the decomposition of proteins, when heated with barium hydroxide, into inactive leucine, tyrosine, and glutamine, whilst at a lower temperature hydrochloric acid produces the active modifications (Ber. **18,** 388). For an experimental explanation of the transformation of optically active substances into their inactive modifications, compare A. Werner in R. Meyer's Jahrbuch der Chemie **1,** 130.

Rotatory Dispersion.—The variation of the specific rotation with the wave-length of the light used is designated *rotatory dispersion*, and in general the rotation increases with decrease in the wave-length (*Normal* rotatory dispersion). If the determinations are carried out with blue and red light, the value $[\alpha]_{\text{blue}} - [\alpha]_{\text{red}}$ is described as the *specific rotatory dispersion*, and the quotient $[\alpha]_{\text{blue}}/[\alpha]_{\text{red}}$ as the *dispersion coefficient*. Biot recognized in 1860 that the rotatory dispersion is a specific property of a substance, and is closely related to its constitution (see *Walden*, Lecture, Ber. **38,** 345 : *Rupe*, Ann. **409,** 334).

(*e*) **Magnetic Rotatory Power.***—Faraday, in 1846, discovered that transparent, isotropic, optically inactive bodies were capable of rotating the plane of polarized light when a column of the substance was brought into the magnetic field, as, for example, when it was surrounded by an electric current. The power of rotation only continued as long as these influences were active, and was reversed when the positions of the magnetic poles were reversed ; this distinguished magnetic rotatory power from the rotatory power of optically active carbon compounds.

Specific magnetic rotatory power is the degree of rotation that the plane of polarization of a ray of light undergoes when it passes through a layer of liquid of definite thickness, exposed to the influence of a magnet. The unit of comparison is the rotation produced by a layer of water of the same temperature and thickness when exposed to the same magnetic field.

Molecular Magnetic Rotatory Power.—This is the degree of rotation produced by columns of liquids chosen of such a length that similar cross-sections will each contain a molecular weight of the substance. The unit in this case can also be the molecular rotatory power of water.

W. H. Perkin, Senior, has investigated minutely the connection between the magnetic rotatory power and the constitution of carbon derivatives. Numerical relations between the increase of rotation and change of composition have been established for many groups of aliphatic and aromatic compounds (C. 1900, I. 797 ; 1902, I. 621 : J.C.S. **105,** 81). Deviations from the theoretical values are encountered particularly in the reactive benzene substitution compounds (see Table, J. pr. Chem. [2] **67,** 334).

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* Graham-Otto, Lehrbuch der Chemie, Vol. I. part 3, p. 793, 1898.

7. ELECTRIC CONDUCTIVITY

Substances which are capable of conducting electricity arrange themselves into two groups : *conductors of the first class*, or those which conduct electricity without undergoing any change, and *conductors of the second class*, known as *electrolytes*, in which conduction is only possible through the agency of the *ions* in which the solutes separate when dissolved. The greater the conductivity of a substance the less is the resistance to the passage of the current ; in other words, the resistance is inversely proportional to the conductivity. The unit of measurement of resistance is the ohm—the resistance of a column of mercury 1·06 metres long, and 1 sq. mm. in cross-section, at 0° C.*

Ostwald's investigations have demonstrated that the conductivity of electrolytes is intimately related to chemical affinity, and forms a direct measure of the chemical affinity of acids and bases. Therefore, the determination of the conductivity of electrolytes (in aqueous solution), to which all organic acids and their salts belong, is of great interest and importance for all carbon derivatives.

Kohlrausch (Wied. Ann. **6**, 1) has suggested a very simple and accurate means of determining the conductivity of electrolytes, which has been extensively applied by Ostwald (J. pr. Chem. **32**, 300, and **33**, 352 ; Z. physik. Chem. **2**, 561). (See also C. 1900, I. 577.) It is dependent on the application of alternating currents, produced by an induction coil, so that the disturbing influence of polarization is avoided.

The conductivity of electrolytes is not referred to the percentage content of their aqueous solutions, but (as the conductivity is determined by the equivalent ions) to solutions containing a gram-molecule, or a gram-equivalent of substance in one litre. This value is the *molecular* (or equivalent) *conductivity* of the substance (Z. physik. Chem. **2**, 567).

The strong acids have the greatest molecular conductivity, and are followed by the fixed alkalis and alkali salts. Most organic acids, on the contrary (*e.g.* acetic acid), are poor conductors in a free condition, whilst their alkali salts approach those of the strong acids in conductivity. The molecular conductivity increases by about 2 per cent. per degree rise of temperature. It also increases with increasing dilution, and in the case of the poor conductors it is far more rapid than with the good conductors ; in both instances it ultimately approaches a maximum (limiting) value. With good conductors this is attained at a dilution of about 1000 litres to the gram-molecule ; whilst with those poor in conducting power it is only reached when the dilution is indefinitely large. In fact, in such cases the conductivity is practically indeterminable.

An interesting observation in connection with the alkali salts of all acids is the variable increase of the molecular conductivity with

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* F. Kohlrausch and Holborn, in their book, " Das Leitungsvermögen der Elektrolyte," adopt as unit a solution of which a column 1 cm. long, and 1 cm.^{2} in section has a resistance of 1 ohm. In this case the conductivity becomes 10,600 times as great as the above. Also, they employ the gram-equivalent in place of the gram-molecule, and the cubic centimetre in place of the litre.

increasing dilution. This is true both in the case of the strong and the weak acids (most organic acids belong to the latter class), and it varies according to their basicity. With sodium salts of monobasic acids, this increase equals from 10–13 units, by dilution from 32 to 1024 litres for the equivalent ; for the salts of dibasic acids from 20–25 units, for those of the tribasic 28–31, for those of the tetrabasic about 40, and those of the pentabasic about 50 units.

Thus it may be seen that the increase in conductivity of acids, in the form of their sodium salts, offers a means of determining the basicity and, consequently, the molecular magnitude of acids (*Ostwald*, Z. physik. Chem. **1**, 74, 97 : **2**, 901 : *Walden*, *ibid.*, **1**, 530 : **2**, 49).

If a certain quantity of an acid be neutralized with $N/32$ sodium hydroxide solution, and the conductivity of the neutral salt be measured before and after dilution to 32 times its volume, the difference of the conductivities divided by 10 gives the basicity of the acid.

Molecular conductivity has acquired still greater importance by its application to the measurement of the dissociation of the electrolytes ; it is at the same time the measure of the reactivity or chemical affinity, first, of acids, then bases, and, finally, of salts.

Arrhenius's electrolytic dissociation theory maintains that in aqueous solution the electrolytes are more or less separated into their ions ; this would give a simple explanation for the variations of solutions from the general laws of osmotic pressure, the depression of the freezing point, etc. (see p. 15). The dissociation is also manifest in the molecular conductivity, for the latter is directly proportional to the degree of dissociation, the number of free ions and the speed of migration of the free ions.

Molecular conductivity increases with dilution and dissociation. When the latter is complete, it attains its maximum (Λ_∞). The degree of dissociation (α) (or the fraction of the electrolyte split up into ions) for any dilution is found from the ratio of the molecular conductivity at this dilution (Λ) to the maximum conductivity (for infinite dilution) :

$$\alpha = \frac{\Lambda}{\Lambda_\infty}.$$

The latter (Λ_∞) cannot be directly measured in the case of free organic acids, because most of them are poor conductors. But it can be obtained from the molecular conductivity of their sodium salts, by deducting from their maximum values ionic mobility of the sodium-ions (49·2), and adding those of the hydrogen-ions (352).

Since the molecular conductivity depends upon the dissociation of the electrolytes into their ions, the effect of dilution must follow the same laws as those prevailing in the dissociation of gases. This influence of dilution or volume (v) upon the molecular conductivity, or the degree of dissociation (α) is, therefore, expressed in the equation :

$$\frac{\alpha^2}{v(1-\alpha)} = \text{K},$$

which represents Ostwald's *dilution law* (Z. physik. Chem. **2**, 36, 270). This law has been fully confirmed by the perfect agreement of the calculated and observed values (*van 't Hoff*, Z. physik. Chem. **2**, 777). In the case of strong electrolytes, such as strong acids and bases, and most salts, the equation of Rudolphi is preferable to that of Ostwald, even though it is empirical : $\frac{\alpha^3}{v(1-\alpha)^2} = \text{K}$.

The value, K, is the same at all dilutions for every monobasic acid ; hence it is a characteristic value for each acid, and is the measure of its chemical affinity. The determination of these chemical *dissociation constants* by Ostwald for more than 240 acids, has proved that they are closely related to the structure and constitution of the bodies (Z. physik. Chem. 3, 170, 241, 369). Literature: see Walden (Z. physik. Chem. 8, 833). Affinity values of stereoisomeric compounds: Hantzsch and Miolatti (Ber. **25**, R. 844).

Determinations of dissociation constants: Conrad, Hecht and *Brückner*, Z. physik. Chem. **3**, 450: **4**, 273, 631: **5**, 289: *Lellmann*, Ber. **22**, 2101; Ann. **260**, 269: **263**, 286: **270**, 204, 208: **274**, 121, 141, 156: *Nernst*, R. Meyer's Jahrbuch **2**, 31: *Jones et al.*, Am. Chem. J. **44**, 159: **50**, 1.

8. PARACHOR

The parachor is a constant for a compound given by the formula

$$[P] = \frac{M}{D - d}\cdot\gamma^{1/4}$$

where M is the molecular weight of a substance, D and d the densities of the liquid and vapour and γ the surface tension. The concept was introduced by Sugden (J.C.S. 1924, **125**, 1185, and subsequent papers: see *Sugden*, The Parachor and Valency, London, 1930) and differs from the ordinary molecular volume in containing a term involving the surface tension, which is related to the internal pressure of the liquid, and thus makes an allowance for the effect of the internal pressure on the molecular volume.

The parachor is a very strictly additive property: the parachor of a compound can be calculated from the parachors of the component atoms, together with definite increments for certain constitutional properties such as multiple bonds, rings, etc. The value for these constants is given in the following table:

C = 4·8
H = 17·1
N = 12·5
O = 20·0
P = 37·7
S = 48·2
F = 25·7
Cl = 54·3
Br = 68·0
I = 91·0

Triple bond = 46·6
Double bond = 23·2
3 membered ring = 16·7
4 membered ring = 11·6
5 membered ring = 8·5
6 membered ring = 6·1

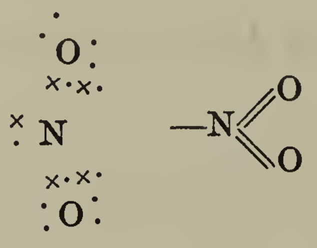
O_2 in esters = 60·0

An example is given of the calculation of the parachor of benzene (Kekulé formula) from the above values:

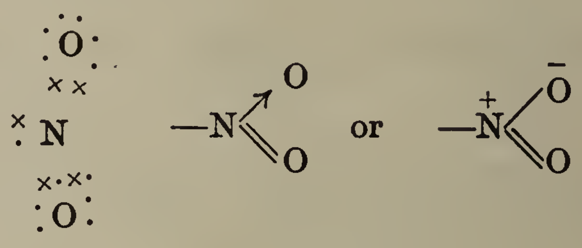
$$\begin{array}{rcrcr} C_6 & = & 6 \times 4{\cdot}8 & = & 28{\cdot}8 \\ H_6 & = & 6 \times 17{\cdot}1 & = & 102{\cdot}6 \\ \text{3 Double bonds} & = & 3 \times 23{\cdot}2 & = & 69{\cdot}6 \\ \text{6 Membered ring} & & & = & 6{\cdot}1 \\ \hline & & \text{Total } [P] & = & \underline{\underline{207{\cdot}1}} \end{array}$$

[P] found experimentally = 206·2.

When compounds containing a double bond are studied, they are found to fall sharply into two classes. In the majority, the parachor determined experimentally agrees well with that calculated from the above figures, allowing an increment of 23·2 for the double bond. A number of compounds, however, instead of this increment, show a decrease of about 1·6 units (Sugden, *op. cit.*, p. 116). It would appear that such compounds, which include nitro compounds, sulphoxides, sulphonates, etc., must contain a double bond of a different nature from that, say, in ethylene. On the electronic theory of valency (p. 29) this type of link is represented as a co-ordinate or semipolar double link, where two atoms are linked by two electrons, both of which are contributed by one atom. The electronic representation of the nitro-group as containing two orthodox double bonds (I) and as containing one ordinary double bond, and one semipolar one (II) is given in the formulæ below.



(I)



(II)

(× = electron contributed by N-atom, · = electron contributed by other atom.)

In (I) the nitrogen is represented as linked to the two oxygen atoms by two ordinary double bonds, each consisting of four electrons, the nitrogen thereby acquiring a share in ten electrons, while the oxygen atoms complete their octets. In (II) one of the N—O bonds is formed by two electrons only, both contributed by the nitrogen, which thereby maintains its (more-stable) octet, while the oxygen octets are simultaneously completed. On the ordinary formula containing two double bonds, the parachor of the nitro group should be given by $N + 2O + 2\,|^{=} = 98{\cdot}9$, while experimentally it is found to be about 73 (Sugden, p. 119), which agrees well with $N + 2O + |^{=} - 1{\cdot}6$ $(= 74)$.

The value of the determination of the parachor for the elucidation of the structure of organic compounds is very great, and in some cases of ring-chain tautomerism (see p. 52: also Sugden, p. 47) the constitution of the stable form of a tautomeric compound can be deduced by the investigation of its parachor.

As regards the physical significance of the parachor, a quotation from Hückel is translated here: "The function formulated upon purely experimental grounds by MacLeod and called the parachor by Sugden is, as to its physical interpretation, quite unexplained, so that it is not known what is really meant by it. Nevertheless, the rules obtained as the result of experiment make it possible to decide questions of constitution."

HEAT OF COMBUSTION OF CARBON COMPOUNDS *

"The quantity of heat evolved in any chemical change is a measure of the total work, both physical and chemical, expended." The determination of the quantity of heat developed in complete combustion is alone adapted for the determination of the energy content of carbon compounds.

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* *Berthelot*, Thermochimie, 2 vols., Paris, 1897. *Plank*, Grundriss der allg. Thermochemie, 1893. *Hans Jahn*, Die Grundsätze der Thermochemie und ihre Bedeutung für die theoretische Chemie, 2. Aufl. 1892. *Ostwald*, Grundriss der allg. Chemie, 1889. *A. W. Roth*, Bestimmung der Verbrennungswärme und ergänzende thermochemische Messungen, Abderhalden's Handbuch der biologischen Arbeitsmethoden, 1927.

The heat of combustion of a carbon compound by the method of Berthelot is determined by combustion with oxygen at a pressure of 25 atmospheres in a calorimetric bomb, lined internally with platinum or enamel. Ignition is effected by means of an electric spark, or by the incandescent products of combustion formed by a thin iron wire heated electrically.

Favre and Silbermann, Thomsen, Stohmann and Berthelot are responsible for the elaboration of methods for the determination of heats of combustion. E. Fischer and F. Wrede have recently brought the method to an extraordinary degree of accuracy (Z. physik. Chem. **69**, 218). *Cf.* also W. A. Roth, Ann. **373**, 249 : **407**, 112.

On the basis of the Hess-Berthelot principle : " The difference of the heats of combustion of two chemically equivalent systems is equal to the heat development which corresponds to the passage of the one system into the other " : it is possible, knowing the heat of combustion of a carbon compound, to calculate its heat of formation. The heat of combustion of the compound is deducted from the sum of the heats of combustion of its elements.

The heat of combustion of methane equals 211·9 *Cal.*
" " diamond-carbon is 94·3 *Cal.*, and
" " hydrogen equals 67·5 *Cal.*

As the complete combustion of methane proceeds according to the equation :

$$CH_4 + 2O_2 = CO_2 + 2H_2O,$$

then the heat of formation of this hydrocarbon, at constant pressure, would be 17·9 *Cal.* :

$$94{\cdot}3 + (2 \times 67{\cdot}5) - 211{\cdot}9 = 17{\cdot}9.$$

Stohmann (Z. physik. Chem. **6**, 334 : **10**, 410) has published a collection of the determinations of heats of combustion made between 1852 and 1892.

The regularities in heats of combustion observed are as follows. In a homologous series, the heat of combustion is increased practically constantly by 154 *Cal.* for each additional CH_2 group (J.A.C.S. **32**, 268). The heat of combustion is, however, not a purely additive property, and isomeric substances do not all possess the same heat of combustion. For instance, the primary alcohols possess a higher heat of combustion than the isomeric secondary and tertiary compounds. Stereoisomeric substances have different heats of combustion : thus fumaric acid has a heat of combustion 6 *Cal.* less than maleic acid, and other pairs of stereoisomeric acids show similar differences (Ber. **46**, 260). The stable *trans*-forms of such acids have in general, not only a lower heat of combustion than the labile *cis*-forms, but also a lower dissociation constant.

The passage of a double bond into two single bonds, or of a triple bond into three singles is associated with a marked loss of energy (Compt. rend. **157**, 895). Compounds with a system of conjugated double bonds show throughout a definitely lower heat of combustion than their isomers with independent double bonds (Ann. **373**, 267 : **385**, 102). The former are more stable compounds than the latter, through a more even valency distribution in the sense of Thiele's theory (p. 28). This explains the tendency of compounds with separated double bonds to pass into their isomers with a conjugated system.

The comparison of the heats of combustion of aromatic substances with their hydrogenated derivatives is interesting in this connection. The difference between benzene derivatives and their dihydro compounds (*c.* 64 *Cal.*) is markedly greater than that between the dihydro and tetrahydro (*c.* 50 *Cal.*) or the tetrahydro- and hexahydro-compounds (*c.* 45 *Cal.*) (Ann. **407**, 145). The breaking of the first double linkage in benzene demands a much larger amount of energy than the breaking of subsequent double bonds : this can be referred to the even valency distribution in benzene, and is responsible for its stability.

The difference in the stability of the *cyclo*propane, *cyclo*butane and *cyclo*pentane rings (see Carbocyclic compounds, Vol. II) which was referred by Baeyer to the variation in the strains of the various rings is also expressed in their varying heats of combustion (J. pr. Chem. [2], **45**, 475 : Ber. **46**, 309 : C. 1913, I. 2026). As an example of the value of the heat of combustion in structural problems, the case of camphoric acid may be cited : the heat of combustion of camphoric acid would appear to exclude the presence of a *cyclo*propane or *cyclo*butane ring, and to demand the presence of a *cyclo*pentane or *cyclo*hexane ring. It should be noted that the differences between the heats of combustion of unsaturated acids and their dimeric polymerization products (*e.g.* acrylic acid, and *cyclo*butanedicarboxylic acid or cinnamic acid and the truxillic acids) is very slight (Z. physik. Chem. **48**, 345).

The investigations of A. v. Weinberg (Ber. **52**, 1501) and Fajans (Ber. **53**, 643) have gone more deeply into the nature of heat of combustion. Using the terminology of the latter, if

x is the heat of formation of a carbon-hydrogen link,
y the heat of formation of a single carbon-carbon bond,
v the heat of formation of liquid water from 1 gm. atom of atomic hydrogen and molecular oxygen,
z the heat of formation of gaseous CO_2 from 1 gm. atom of monatomic carbon vapour and molecular oxygen,

the heat of combustion of a substance, *e.g.* of propane, C_3H_8, can be represented by an equation

$$-8x - 2y + 8v + 3z = 526{\cdot}7 \textit{ Cal.} \text{ per Mol.}$$

The value v can be calculated as 74·4 by making use of the heat of dissociation of hydrogen: similarly, z can be calculated as 381 *Cal.* by reference to the heat of sublimation of carbon. Employing these values,

x denotes the absorption of 117 *Cal.* in the formation of a C—H bond,
y denotes the absorption of 137·5 *Cal.* in the formation of a single C—C bond.

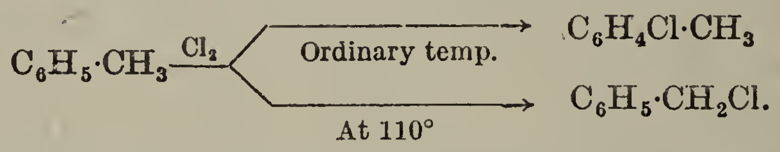
These determinations show that the energy content of a C—C link in an aliphatic compound and in diamond (*c.* 140 *Cal.*) are very similar, and not very different from that of a C—H link (117 *Cal.*): on this basis, diamond may be regarded as the basic substance of the aliphatic compounds.

ACTION OF HEAT, LIGHT, AND ELECTRICITY UPON CARBON COMPOUNDS

1. ACTION OF HEAT

Substances which react most energetically upon each other do not do so at very low temperatures (*Raoul Pictet*, Arch. d. Scienc. phys. et nat., Geneva, 1893), even when subjected to the greatest pressure, and when their molecules are in most intimate contact. A definite temperature is essential for the occurrence of chemical action. The energy of a reaction, the time within which it proceeds, is largely dependent on the temperature of the reacting substances, therefore the determination of the most favourable temperature for the reaction is important. It must be remembered that the heat developed in chemical changes frequently increases the initial reaction-temperature rapidly to the point of decomposition. In such cases the violence of the reaction must be moderated by cooling or by the use of indifferent diluents, in which the substances acting upon each other must be dissolved before the reaction occurs.

The action of chlorine upon toluene (*q.v.*) shows particularly well how much the kind and nature of the action is dependent upon the temperature. At the ordinary temperature the chlorine substitutes the hydrogen of the benzene nucleus, whilst at the boiling temperature it is the hydrogen of the methyl group which is replaced:



Numerous analogous observations are known.

In general, carbon compounds are much less stable under the influence of heat than the inorganic bodies. When the qualitative examination of organic bodies was discussed, mention was made of the fact that many carbon compounds were decomposed under the influence of heat with the separation of carbon.

Other compounds, when heated at the ordinary temperature, re-arrange themselves without alteration of their molecular magnitude, whilst some polymerize. Compounds, volatilizing undecomposed at ordinary pressure, may become decomposed when their vapours are conducted through tubes heated to redness, or by contact with metallic wires rendered incandescent by the electric current (C. 1901, II. 1042); as a rule, new bodies are then formed accompanied by partial carbonization. The splitting-off of hydrogen, the halogens, haloid acids, water, and ammonia leads to a more intimate union of the already combined carbon atoms, and carbon atoms which previously were not united with one another not infrequently combine to yield carbocyclic and heterocyclic bodies: pyro-condensations result (Ber. **11**, 1214).

In the special part of this volume, such results from heat action will be so frequently encountered that it becomes unnecessary to present examples at this time (*cf.* ethyl alcohol and chloroform).

It may suffice to mention coal tar, which contains the liquid bodies formed by the decomposition of coal under the influence of heat. This material is of the greatest importance both in the development of scientific, theoretical organic chemistry, as well as for technical chemistry (coal-tar industry). It is mainly composed of carbo- and heterocyclic compounds, stable under the influence of heat:

C_6H_6 Benzene.
$C_{10}H_8$ Naphthalene.
$C_{14}H_{10}$ Anthracene, Phenanthrene.
C_4H_4S Thiophene.
C_5H_5N Pyridine.
C_9H_7N Quinoline and *iso*Quinoline.
$C_{13}H_9N$ Acridine.

See also pyrogenic acetylene-condensations, *R. Meyer*, Ber. **46** to **53**.

2. ACTION OF LIGHT

Light exerts a great influence upon carbon compounds. The well-known reactions of this kind in the field of inorganic chemistry have corresponding cases in the province of organic chemistry.

Light is able to bring about the decomposition, the rearrangement, and the synthesis of carbon bodies. Just as the haloid salts of silver are decomposed with separation of silver, so, too, the *alkyl iodides* separate iodine under the influence of light. Hence their colourless solutions gradually become yellow and finally dark brown in colour. Ethyl mercuric iodide breaks down into mercurous iodide and butane. Experience shows that many other carbon derivatives decompose more or less rapidly when they are exposed to sunlight, hence they must be preserved in the dark or in vessels of brown-coloured glass, which absorbs the chemically active rays of sunlight. It is technically important that an organic dye should resist the influence of light; most of them are not fast colours, but are bleached by light.

Of the decomposition-reactions produced by sunlight mention may be made of the change undergone by *succinic acid*, when mixed with uranium oxide ; it loses carbon dioxide, and propionic acid results (Ann. **133**, 253) :

$$CO_2H{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H = CO_2 + CH_3{\cdot}CH_2{\cdot}CO_2H.$$

Solutions of *tartaric acid* and *citric acid*, when mixed with uranium oxide, are similarly decomposed by sunlight (Ann. **278**, 373).

An aqueous solution of *acetone* is partially hydrolized by sunlight into acetic acid and methane (Ber. **36**, 1582).

Mercury oxalate is decomposed by light into CO_2 and mercury ; if ammonium chloride be present, calomel is formed. A similar reaction is the following :

$$2HgCl_2 + C_2O_4(NH_4)_2 = Hg_2Cl_2 + 2CO_2 + 2NH_4Cl.$$

Sunlight often acts as a polymerizing agent. Solid *anthracene*, in the form of a vapour or solution, is polymerized by sunlight or the light of a carbon or mercury arc lamp into dianthracene, a change which is completely reversed in the dark (Z. physik. Chem. **53**, 385). For similar cases of *phototropy* see Ber. **37**, 2236.

Finely divided *cinnamic acid* changes in sunlight to the dimeric *truxillic acid*, which returns to the simpler form under the influence of heat ; cinnamylidene malonic acid behaves in the same way (Z. physik. Chem. **48**, 345).

For the polymerization of *benzaldehyde* see Ber. **36**, 1573.

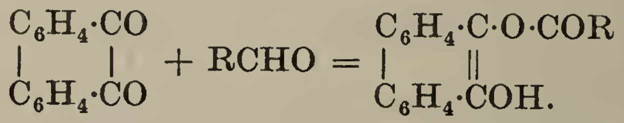
Geometric isomers (alloisomers or stereoisomers) are frequently changed into their stable forms by sunlight ; for instance, maleic acid into fumaric acid (Ber. **36**, 4267), *allo*cinnamic acid into cinnamic acid ; *anti*-oximes into *syn*-oximes (Ber. **36**, 4268 : **37**, 180).

The combination of *carbon monoxide* and *chlorine*, forming carbonyl chloride or phosgene (*Davy*), is analogous to the complete union of hydrogen and chlorine, forming hydrogen chloride, and of benzene and chlorine or bromine to form hexa-chloro- or hexabromo-benzene, in sunlight :

$$H_2 + Cl_2 = 2HCl\,;\quad CO + Cl_2 = COCl_2\,;\quad C_6H_6 + 3Cl_2 = C_6H_6Cl_6.$$

The action of chlorine upon methane (p. 93), formaldehyde (Ber. **29**, R. 88), and other carbon derivatives which can be substituted, is much influenced by sunlight.

The experiments conducted by Klinger show that the chemical action of sunlight is susceptible of more extended application than it has yet found, and that compounds can be produced by it, which could only be prepared in the ordinary chemical way by most powerful or highly specialized means. He found that ethereal solutions of benzoquinone, benzil, and phenanthraquinone are reduced, with the formation of aldehyde. Further, that acetaldehyde, *iso*valeraldehyde, and benzaldehyde unite, under the influence of sunlight, with phenanthraquinone, in accordance with the equation (Ann. **249**, 137) :



$$\begin{array}{l} C_6H_4{\cdot}CO \\ |\qquad\; | \\ C_6H_4{\cdot}CO \end{array} + RCHO = \begin{array}{l} C_6H_4{\cdot}C{\cdot}O{\cdot}COR \\ |\qquad \| \\ C_6H_4{\cdot}COH. \end{array}$$

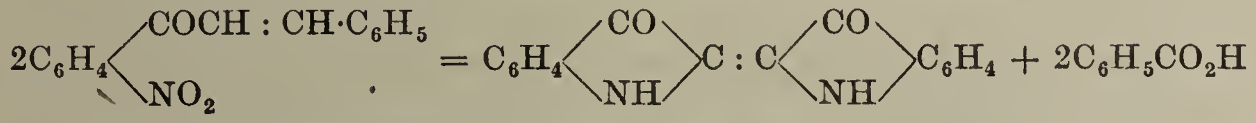
*iso*Valeraldehyde and benzaldehyde also unite directly with benzoquinone, but in a still more striking manner, in that a nucleus-synthesis (p. 97) results. With benzaldehyde the reaction proceeds as follows :—

$$\underset{\text{Benzo-quinone.}}{C_6H_4O_2} + \underset{\text{Benz-aldehyde.}}{C_6H_5{\cdot}COH} = \underset{\text{Dihydroxybenzophenone.}}{C_6H_5{\cdot}CO{\cdot}C_6H_3(OH)_2}$$

Sunlight reduces a carbonyl group in alcoholic solution, and at the same time the alcohol becomes oxidized to aldehyde, as, for instance, benzophenone and acetophenone yield the corresponding pinacones ; quinone oxidizes glycerol to glycerose, erythritol to erythrose, mannitol to mannitose, dulcitol to dulcitose, dextrose to dextrosone, whilst in each case the quinone changes to quinhydrone.

Aromatic nitro-bodies readily give up their oxygen to alcoholic or aldehydic groups under the influence of sunlight : nitrobenzene and alcohol give aniline and quinaldine ; nitrobenzene and benzaldehyde yield a mixture of benzoic acid, nitrosobenzene, *β*-phenylhydroxylamine and products of further interaction ; *o*-nitrobenzaldehyde changes completely into *o*-nitrosobenzoic acid ; *o*-nitro-benzal aniline gives *o*-nitrosobenzanilide, and so on (*Ciamician* and *Silber*, Ber. **37**, 3425 : **38**, 1176, 3813).

o-Nitrobenzylidene acetophenone in ethereal solution is changed by sunlight to indigo and benzoic acid (*Engler* and *Dorant*, Ber. **28**, 2497) :



$$2C_6H_4\left\langle\begin{matrix}COCH:CH\cdot C_6H_5\\NO_2\end{matrix}\right. = C_6H_4\left\langle\begin{matrix}CO\\NH\end{matrix}\right\rangle C:C\left\langle\begin{matrix}CO\\NH\end{matrix}\right\rangle C_6H_4 + 2C_6H_5CO_2H$$

The study of these reactions is specially important in the interpretation of the chemical changes occurring in plants.

3. ACTION OF ELECTRICITY

Some of the reactions induced by the aid of electricity possess great value for synthetic organic chemistry. The only method which will cause the union of free hydrogen with free carbon, consists in the action of the electric discharge upon the two elements. Berthelot showed that carbon and hydrogen combined to form acetylene on the passage of the electric spark between carbon points in an atmosphere of hydrogen: $2C + H_2 = CH\equiv CH$. Small quantities of methane CH_4, and ethane C_2H_6 were also present, as was found later (C. 1901, II. 576). Fig. 14 represents the apparatus in which this important synthesis was carried out (Ann. chim. phys. [4] **13, 143** : Ber. **23,** 1638 : C. 1897, I. 24).

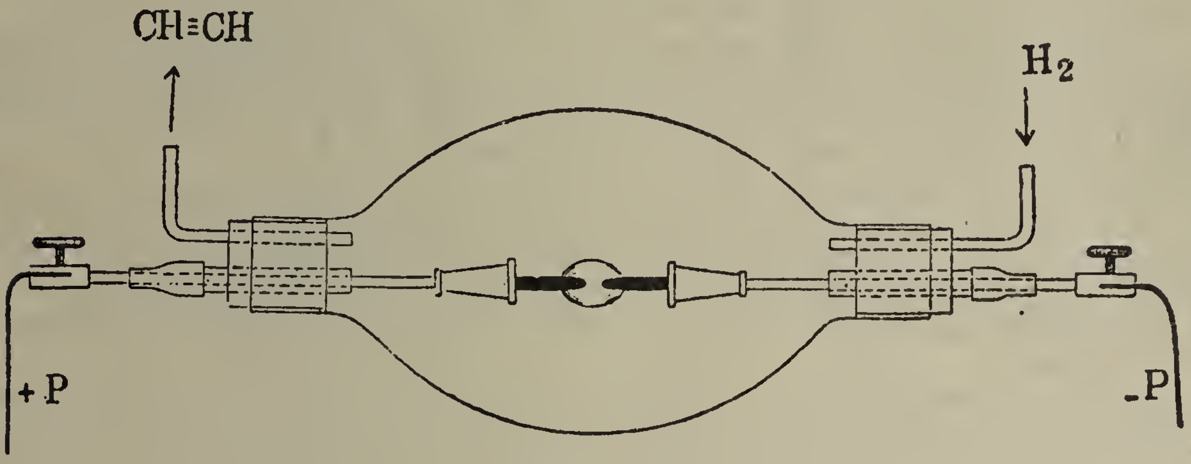
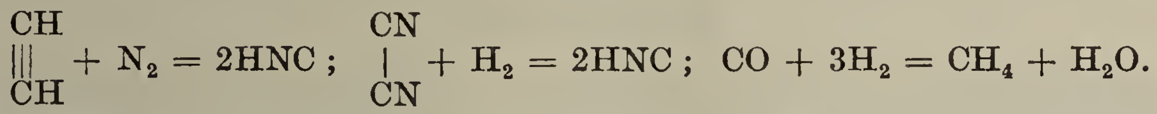


Fig. 14.

Acetylene and nitrogen (Ann. **150**, 60) as well as cyanogen and hydrogen, unite to yield hydrocyanic acid under the influence of electric discharges (Compt. rend. **76**, 1132) ; and carbon monoxide and hydrogen form methane (Brodie, Ann. **169**, 270).



$$\begin{matrix}CH\\|||\\CH\end{matrix} + N_2 = 2HNC;\quad \begin{matrix}CN\\|\\CN\end{matrix} + H_2 = 2HNC;\quad CO + 3H_2 = CH_4 + H_2O.$$

An important application of the heat derived from electricity is the preparation of the carbides in the electric furnace (*Moissan*),* where temperatures of about 3000° can easily be reached. Calcium and aluminium carbides are of the greatest significance to organic chemistry, because water liberates from them acetylene and methane respectively (comp. p. 86).

Other thermal reactions can also be effected, such as passing the vapours of carbon compounds over a metallic spiral heated to incandescence by an electric current (C. 1901, II. 1042 : see also Ber. **18**, 3350).

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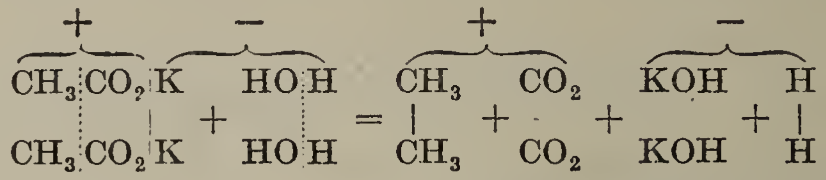
* *Moissan,* Le four électrique, Paris, 1897.

Kolbe decomposed the aqueous solutions of the potassium salts of monobasic carboxylic acids, especially potassium acetate, by the electric current, and thus prepared dimethyl or ethane. The following equation represents the electrolysis of potassium acetate :



$$\overbrace{\begin{matrix}CH_3 \vdots CO_2\\ \vdots \quad | \\ CH_3 \vdots CO_2\end{matrix}}^{+}\overbrace{\begin{matrix}K\\ \\ K\end{matrix} + \begin{matrix}HO\\ \\ HO\end{matrix}}^{-}\begin{matrix}\vdots H\\ \vdots\\ \vdots H\end{matrix} = \overbrace{\begin{matrix}CH_3\\ |\\ CH_3\end{matrix} + \begin{matrix}CO_2\\ \\ CO_2\end{matrix}}^{+} + \overbrace{\begin{matrix}KOH\\ \\ KOH\end{matrix} + \begin{matrix}H\\ |\\ H\end{matrix}}^{-}$$

Kekulé applied this reaction to the saturated dicarboxylic acids, *e.g.* succinic acid, and later he and Aarland extended it to the unsaturated dicarboxylic acids : fumaric acid, maleic acid, mesaconic acid, citraconic acid, and itaconic acid (Ann. **131**, 79 : J. pr. Chem. [2] **6**, 256 : **7**, 142 : comp. C. 1900, I. 1057 : II. 171), with the production of the unsaturated hydrocarbons, ethylene, acetylene, and allylene. Kolbe and Moore obtained ethylene dicyanide from cyanacetic acid (Ber. **4**, 519). Crum Brown and J. Walker included the potassium salts of the acid esters of the dicarboxylic acids among these reactions, and obtained the neutral esters of dibasic acids, *e.g.* potassium ethyl malonate yielded succinic diethyl ester (Ann. **261**, 107 : Ber. **24**, R. 36 : Ann. **274**, 41 : Ber. **26**, R. 369, 380). In the electrolysis of an alcoholic solution of sodium malonic diethyl ester Mulliken obtained ethanetetracarboxylic ester (Ber. **28**, R. 450).

V. Miller and Hans Hofer showed that by electrolysis of potassium acetate and potassium ethyl succinate, butyric ester is formed (Ber. **28**, 2429). Mulliken obtained ethanetetracarboxylic ester by electrolysis of an alcoholic solution of sodium malonic diethyl ester (Ber. **28**, R. 450).

Hamonet obtained the diamyl ether of butane-diol by the electrolysis of the amyl ether of potassium β-hydroxypropionate (C. 1901, I. 613). From the salts of ketocarboxylic acids, either alone or mixed with acetates, Hofer obtained by electrolysis ketones and diketones : pyroracemic acid yields diacetyl ; lævulinic acid gives octane-βη-dione, pyroracemic acid and acetic acid yield acetone (Ber. **33**, 650).

Hydrogen, generated by electrolysis, is a valuable means for reducing organic substances, as its action can be varied according to the liquid, current, voltage, cathode material, etc., employed for the particular requirements of the experiment. Aromatic nitro-bodies can be changed into their various reduction products—β-phenylhydroxylamines, aminophenol, azoxy- azo- or hydrazo-bodies, or into anilines (Ber. **28**, 2349 : **29**, 1390 : **38**, 3076). Many substances which are difficult to reduce by chemical methods, such as carboxyl groups in ketones, carboxylic acids and their esters, lactams, dicarboxylic acid imides, and others, can easily be reduced to CHOH or CH_2 groups in sulphuric acid solutions with cathodes possessing a high overvoltage (Cd, Hg, Pb) (*Tafel*, Ber. **33**, 2209 : **37**, 3187, etc. : Ann. **348**, 199).

Similarly, oxygen at the anode can be used for the electrolytic oxidation of organic compounds (Helv. Chim. Acta. **4**, 928, 1000 : **5**, 60, 166 : Z. Elektrochem. **27**, 487).

THE DIRECT COMBINATION OF CARBON WITH OTHER ELEMENTS

Before dealing with the systematic classification of the carbon compounds, some remarks may be made, by way of introduction, on the direct combination of carbon with other elements. Carbon and its various allotropic modifications are described in text-books on inorganic chemistry, but its affinity to other elements may well be discussed here also, since from the substances formed by direct union with other elements the innumerable compounds in organic chemistry are derived.

With one exception the combining power of carbon becomes operative only at high temperatures. In the finely-divided form of soot, carbon will combine with fluorine, to form tetrafluoromethane or carbon tetrafluoride

$$C + 2F_2 = CF_4.$$

Combination with hydrogen or chlorine can only be brought about under the influence of the electric arc, when carbon and hydrogen unite to form acetylene, the most reactive of all hydrocarbons, together with a little methane (p. 91) :

$$2C + H_2 = C_2H_2, \qquad C + 2H_2 = CH_4;$$

and chlorine and carbon combine to form hexachlorethane and perchlorobenzene :

$$2C + 3Cl_2 = C_2Cl_6; \qquad 6C + 3Cl_2 = C_6Cl_6.$$

Oxygen unites with carbon, producing carbon monoxide and carbon dioxide or carbonic acid gas :

$$C + O = CO; \qquad C + O_2 = CO_2.$$

Which of these two substances is formed depends on the temperature of reaction. At very high temperatures only carbon monoxide is formed, the dioxide being produced below this. The affinity of carbon for oxygen is so great that at sufficiently high temperatures the most stable oxides give up their oxygen, so that carbon becomes the most important reducing agent for technical purposes.

Sulphur combines with carbon at high temperatures in only one proportion forming carbon disulphide—the sulphur analogue of the anhydride of carbonic acid :

$$C + S_2 = CS_2.$$

The formation of C_4S in this reaction is not definitely proved (Z. angew. Chem. **40**, 1136).

It is not yet decided whether a direct union of carbon and nitrogen takes place in the arc with formation of cyanogen (Compt. rend. **151**, 1057, 1328).

Carbon, nitrogen, and hydrogen combine together when a mixture of nitrogen and hydrogen is passed between carbon poles of an electric arc, forming hydrocyanic acid, a reaction which possibly depends on the primary formation of acetylene :

$$C + N + H = HNC,$$
$$\text{or } 2C + 2H = C_2H_2 \text{ and } C_2H_2 + N_2 = 2HNC.$$

Similarly, carbon, nitrogen, and potassium or sodium, combine at high temperatures to form potassium or sodium cyanide. This reaction may also depend on the primary formation of potassium or sodium acetylide, followed by subsequent union with nitrogen. Or a metallic nitride may first be formed which then combines with carbon to produce the cyanide.

At very high temperatures carbon exhibits the capacity of combining directly with many elements of a metallic character to form carbides. Even in the early days the formation of iron carbide was proved to take place by the action of carbon on molten iron.

However, pure iron carbide is not known, but it appears that carbon combines with iron in various proportions. This is supported by the generation of a mixture of hydrocarbons when such a specimen of iron is dissolved in acids.

Carbon unites with the metals of the alkaline earths, calcium, strontium, and barium, in only one proportion. Such a carbide can be considered as being a metal-acetylene compound, which generates the gas on contact with water. It is prepared by the reduction of the oxide of the metal by carbon in the electric furnace :

$$3C + CaO \longrightarrow CaC_2 + CO.$$

Aluminium carbide, similarly prepared, gives off methane in contact with water :

$$3C + 4Al = C_3Al_4.$$

Beryllium carbide also yields methane ; manganese carbide generates equal volumes of methane and hydrogen ; the carbides of cerium, lanthanum, yttrium, samarium, C_2M give acetylene and methane ; uranium carbide, C_3U_2 yields methane, hydrogen, and ethylene ; whilst the last-named carbides also yield large amounts of liquid and solid hydrocarbons (Compt. rend. **122**, 1462, etc.). Magnesium forms two carbides, MgC_2 and Mg_2C_3. With water the first yields acetylene, the second allylene (Z. physik. Chem. **73**, 513).

Whilst the carbides of the enumerated metals give off hydrocarbons when treated with acids or water, the carbides of boron, silicon, titanium, zirconium, vanadium, tungsten and chromium are extraordinarily stable and unusually hard ; so much so that silicon carbide is employed, under the name of carborundum, in boring and polishing. The last three carbides are so far useless in the building up of carbon compounds.

The most important substances which have been formed by the direct union of carbon with other elements are :

Acetylene	C_2H_2
Calcium carbide	C_2Ca
Methane	CH_4
Aluminium carbide	C_3Al_4
Carbon monoxide	CO
Carbon dioxide	CO_2
Carbon disulphide	CS_2
Hydrocyanic acid	HNC
Potassium cyanide	KNC

These bodies are examples of widely different classes of organic compounds ; methane and aluminium carbide are found at the head of the paraffin or acyclic saturated hydrocarbons, whilst acetylene and calcium carbide occupy a similar position among the unsaturated acyclic hydrocarbons possessing a triple bond between two carbon atoms. Carbon monoxide, hydrocyanic acid and potassium cyanide will be described with formic acid derivatives : carbon dioxide and disulphide as derivatives of carbonic acid before the paraffin dicarboxylic acids.

Of all these simple compounds of carbon, the most important is carbon dioxide, which forms the basis for the formation of the carbohydrates and fats during the process of assimilation in the vegetable organism ; and also of the proteins when nitrogen is taken up.

Since chemists have not yet succeeded in imitating in the laboratory the synthetic methods of plants, a large and increasing number of methods have been provided for linking together simple organic molecules for the construction of substances of complicated composition. These methods depend partly on double decomposition, similar to the interaction of inorganic salts, but mainly on the property of one " unsaturated " molecule (p. 27) to unite with another ; on reactions brought about by the agency of metals, especially Na, Mg, Al, Zn, Cu, or suitable compounds of them ; on the influence of acids ; and finally on rise of temperature, on sunlight or on electricity (pp. 80–84).

CLASSIFICATION OF THE CARBON COMPOUNDS

The chemical union of the carbon atoms and the resulting character of the groups is the basis of the division of the carbon compounds into two principal classes : the **fatty** or **aliphatic substances** (from ἄλειφαϱ, fat)—the chain or acyclic carbon derivatives or the methane derivatives, and the **cyclic compounds** of carbon.

The name of the first class is borrowed from the fats and fatty acids comprising it, which were the first derivatives to be studied accurately. They may be termed the marsh gas or *methane derivatives*, inasmuch as they all can be derived ultimately from methane, CH_4. They are further classified into *saturated* and *unsaturated* compounds. In the first of these, called also paraffins, the directly united quadrivalent carbon atoms are linked to each other by a single bond, so that the number of affinities still remaining to be satisfied in a chain of n carbon atoms is $2n + 2$ (p. 33). Their general formula is, therefore, expressed in the form C_nX_{2n+2}, where X represents the affinities of the elements or groups directly combined with carbon. The unsaturated compounds result from the saturated by the loss of an even number of affinities in union with carbon. According to the number of affinities yet capable of saturation, the series are distinguished as C_nX_{2n}, C_nX_{2n-2}, etc.

The *methane derivatives* contain open carbon chains, the *cyclic derivatives* contain closed carbon chains, or rings. When carbon atoms alone constitute the ring, the resulting bodies are designated *carbocyclic compounds.*

Especially important among these cyclic compounds are those in which the ring contains six carbon atoms with six free valencies. From these are derived substances which Kekulé named the *aromatic compounds* or *benzene derivatives.*

The importance of this group has gained for it a special position in the chemistry of carbon derivatives. Compared with the aliphatic compounds, they show such great differences in chemical behaviour that they were formerly regarded as a second and distinct class of organic bodies.

With the advances in organic chemistry, numerous compounds were being constantly discovered which contained carbon atoms united in a closed ring, but which approached the fatty bodies more closely than the aromatic derivatives in chemical behaviour. In the so-called hydroaromatic compounds the more pairs of hydrogen atoms which are attached to the benzene nucleus in them, the nearer they resemble, in chemical character, the aliphatic derivatives. Even more closely allied to the latter are those substances which contain a ring consisting of three, four, or five carbon atoms—

the *trimethylene* or *cyclo*propane derivatives,
tetramethylene or *cyclo*butane derivatives,
pentamethylene or *cyclo*pentane derivatives.

These constitute the passage from the aliphatic bodies to the *hydro-aromatic* compounds or *cyclo*hexane derivatives, with which the *aromatic* derivatives are so closely connected.

There are many carbon compounds containing "rings," in the formation of which not only carbon atoms, but also oxygen, sulphur, and nitrogen atoms take part.

Such bodies have been termed *heterocyclic compounds* (from ἕτερος, foreign). These derivatives will mainly be discussed at the conclusion of the remarks on the open chain bodies, from which they are derived by loss of water, hydrogen sulphide, or ammonia, and into which they can again be changed. A large class of heterocyclic bodies, the thiophen, furan, and pyrrole groups: the parent substances of the plant alkaloids, pyridine, quinoline, *iso*quinoline, etc.—like the aromatic bodies, possess very stable rings. In the case of many heterocyclic bodies the open chain compounds, from which they may theoretically be deduced, do not actually exist. Therefore such heterocyclic compounds will be more conveniently discussed after the carbo- or isocyclic derivatives. Thus, the chemistry of the compounds of carbon may be divided into:

I. Fatty Compounds: *Aliphatic compounds, methane derivatives, chain or acyclic carbon derivatives.*

II. Carbocyclic Compounds.

III. Heterocyclic Compounds.

THE NOMENCLATURE OF THE CARBON COMPOUNDS

The steadily increasing number of carbon derivatives has shown the necessity that definite principles should determine their designation. The absence of such general and international rules (where they were possible) has led to great confusion in the nomenclature.

Compounds originating from plants and animals received names that indicated their origin, and often at the same time their characteristic chemical properties: urea, uric acid, tartar, tartaric acid, formic, oxalic, malic, citric, salicylic acids, etc. With a large class of bodies, *e.g.* the bases, glucosides, bitter principles, fats, etc., it was customary to employ the ending "ine": coniine, nicotine, guanidine, creatine, betaine, salicine, amygdaline, glycerine, stearine, etc., and in the terminations al, ol, an, en, yl, ylene, ylidene, the effort was made to show the similarity of certain compounds, without, however, proceeding in a systematic way.

The more thoroughly the constitution of bodies became known, the greater was the desire to indicate by names the manner in which the atoms were united. This was especially true in the case of isomeric compounds. The manner in which this was done, however, was left to the choice of the individual, and thus it happened that often one and the same derivative received different names, which possessed fundamentally equivalent meanings.

Of the early suggestions on nomenclature, that of *Kolbe* (Ann. **113**, 307) on *carbinol* deserves special consideration. As is known, Kolbe referred the names of the monohydroxy saturated alcohols back to the name *carbinol*. In order to make this principle more general, it becomes necessary to ascertain the "carbinol" or " carbinols " for each class of compounds—that is, to find those bodies from which the homologues might be derived, just as the monohydroxy saturated alcohols might be deduced from methyl alcohol or carbinol. Without attempting at this time to determine the limits of the " carbinol nomenclature," it will suffice to remark that in the case of the paraffin dicarboxylic acids all the normal homologues are the " carbinols," *e.g.* malonic acid, succinic acid, normal glutaric acid, adipic acid, etc. Indeed, names such as monomethylmalonic acid, ethylmethylmalonic acid, symmetric and unsymmetric dimethylsuccinic acid, etc., are so readily understood that they are preferred by many chemists.

In order to minimize as far as possible the arbitrary nomenclature of organic compounds, a meeting was convened in Geneva, in 1892, of the chemists of nearly all the civilized countries, for the purpose of agreeing on a method of indicating the constitution of carbon compounds in a consistent and clear manner. The new " official " names adopted by the Geneva Convention will, in the case of certain important series of compounds, be observed in the present text ; they will be enclosed in brackets—*e.g.* [ethene] for ethylene, [ethine] for acetylene, etc. The designations of the simpler bodies—the names justified from an historical standpoint and deduced from important reactions—will not be wholly eliminated. Thus, the names ethyl hydride, dimethyl or methylmethane will be used for ethane, depending upon what relations are especially to be emphasized.

The new nomenclature proceeds from, or begins with, the hydrocarbons. The name of the hydrocarbon serves as the *root* for the names of those substances which contain their carbon atoms arranged in a similar manner. The different classes of bodies are distinguished by the addition of suffixes to the names of the hydrocarbons : alcohols end in *ol*, aldehydes in *al*, ketones in *one*, and the acids in *acid*—*e.g.* [ethanol] = ethyl alcohol, [ethanal] = acetaldehyde, [propanone] = acetone, [propanal] = propionic aldehyde, [ethane-acid] = acetic acid. These examples will suffice. The more detailed consideration will be given to the various classes of bodies which are discussed. The principles of this nomenclature have already been found difficult of application, especially in attempting to indicate in name a compound having a mixed character—*e.g.* the body $COH—CH_2—CHOH—CO—CO_2H$, which would be *pentanolalone-acid*. The accumulation of suffixes, each of which possesses a meaning peculiar to itself, has " conduit rapidement à des termes bizarres, d'une complication facheuse et d'une prononciation difficile " (Amé Pictet).

For the decisions of the International Congress of Geneva, convened 19th to 22nd April, 1892, for the purpose of co-ordinating chemical nomenclature, see Tiemann (Ber. **26**, 1595) : Istrate's proposals (C. 1898, I. 17). On the nomenclature of ring-compounds, see Vol. II ; also M. M. Richter (Ber. **29**, 586).

In order to distinguish the more frequently occurring radicals of the same kind, such as the univalent hydrocarbon residues, both aliphatic and aromatic, the name *alkyl* has been accepted. In differentiating between the two classes *alphyl* refers to the aliphatic residues and *aryl* to the aromatic ; whilst aromatic residues possessing aliphatic characteristics are referred to as *alpharyl*. Carboxylic acid residues, too, are referred to as *acyl* and differentiated into *alphacyl* and *aracyl* (C. 1899, I. 825). Schlossberger has suggested that the names of acid radicals should end in " *oyl* " similarly to benzoyl : thus acoyl, alphacoyl and aracoyl groups may be spoken of (Ann. **439**, Anm. 3).

A revised code of rules for the nomenclature of organic compounds was drawn up in 1931 by the International Union of Chemistry, and these are published in J.C.S. **1931**, 1607. It is recommended that arabic numerals be used throughout for the numbering of carbon chains, but in this edition the older custom of using Greek letters for numeration of open chains, and arabic numerals for rings has been systematically followed, with the exception of sugar derivatives, where the use of arabic numerals has been customary for some time.

I. FATTY COMPOUNDS, ALIPHATIC SUBSTANCES OR METHANE DERIVATIVES, CHAIN OR ACYCLIC CARBON DERIVATIVES

1. HYDROCARBONS

The hydrocarbons may be regarded as the parent substances from which all other carbon compounds arise by the replacement of the hydrogen atoms by different elements or groups.

We distinguish (1) *saturated* and (2) *unsaturated hydrocarbons.* The first contain only singly linked carbon atoms, whilst the unsaturated contain pairs of carbon atoms united doubly and trebly. The saturated series is usually referred to as the methane series or the paraffins (paraffin is derived from *parum affinis* in reference to their lack of reactivity).

A. SATURATED HYDROCARBONS

(Paraffins or Methane Hydrocarbons)

Methods of Formation and Properties of the Paraffins.—The saturated hydrocarbons are formed in the dry distillation of wood, peat, bituminous shale, brown coal, coal, particularly the boghead and cannel coal rich in hydrogen ; hence they are present in illuminating gas and in the light oils of coal-tar. They occur already formed in petroleum, particularly in that from America, which consists almost exclusively of them, and contains most members from methane to the highest. It is difficult to isolate the individual hydrocarbons from such mixtures. Before advancing to the general methods used in the preparation of the paraffins—methods by which each separate member can be easily obtained in pure condition—it will be best to discuss the two important bodies, methame and ethane.

(1) **Methane,** *Methyl Hydride, Marsh Gas,* CH_4, is produced in the decay of organic substances ; it is, therefore, disengaged in swamps (marsh gas) and mines, in which, mixed with air, it forms fire-damp.

In certain regions, like Baku in the Caucasus and the petroleum districts of America, it escapes, in great quantities, from the earth. It is also present, in appreciable amount, in illuminating gas. A borehole sunk to 247 metres deep near Hamburg in 1910 yielded gas containing 91 per cent. of methane.

The synthesis of methane, the simplest hydrocarbon, from which all the fatty bodies may be derived, is particularly important. By the synthesis of a carbon compound is understood its formation from the elements, or from such carbon derivatives which can be obtained from the elements. Under proper conditions hydrogen and carbon may be directly combined, with the production of acetylene $CH{\equiv}CH$ (p. 83), together with only a small quantity of methane. The latter can be obtained (1) from carbon disulphide CS_2 (which may also be made directly from its constituents) (*a*) if the vapours of this volatile substance, mixed with hydrogen sulphide gas, be passed over red-hot copper (*Berthelot*):

$$C + 2S = CS_2; \qquad CS_2 + 2H_2S + 8Cu = CH_4 + 4Cu_2S.$$

Or (*b*) the carbon disulphide may be converted by chlorine into carbon tetra-chloride CCl_4, and this reduced, by nascent hydrogen (sodium amalgam and water):

$$CS_2 + 3Cl_2 = CCl_4 + S_2Cl_2; \qquad CCl_4 + 8H = CH_4 + 4HCl.$$

(2) Methane is also formed from carbon monoxide and hydrogen, if the mixture of gases be exposed in an induction tube to the action of electricity (p. 83), (Ann. **169,** 270), or is led over freshly reduced nickel (Compt. rend. **134,** 514):

$$2C + O_2 = 2CO \qquad CO + 3H_2 = CH_4 + H_2O.$$

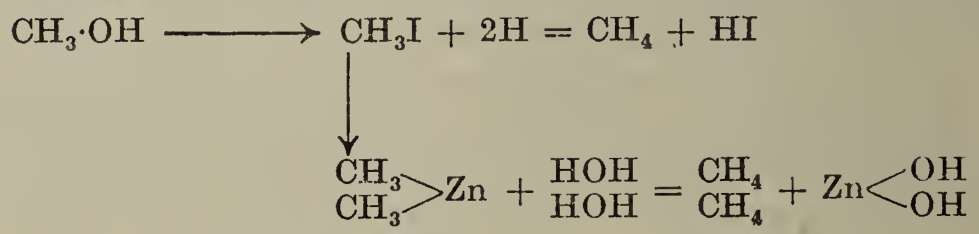
Methane is also obtained quantitatively from carbon monoxide and excess of water vapour, when the mixture is led over a nickel catalyst at 275° (Compt. rend. 1930, **191,** 186):

$$4CO + 2H_2O = 3CO_2 + CH_4.$$

(3) Aluminium carbide is decomposed, in the cold, by water, forming methane and aluminium hydroxide (Ber. **27,** R. 620: **29,** R. 613):

$$C_3Al_4 + 12H_2O = 3CH_4 + 2Al_2(OH)_6.$$

(4) Methyl alcohol or wood-spirit, $CH_3{\cdot}OH$, can be converted into methane by first changing it to methyl iodide, and then reducing the latter with nascent hydrogen from moist zinc-copper, or with zinc dust in the presence of alcohol (Ber. **9,** 1810), or with potassium hydride (C. 1902, I. 708), or by preparing zinc methyl, $Zn(CH_2)_2$, from methyl iodide, and decomposing it with water:



$$\begin{tikzcd}
CH_3{\cdot}OH \arrow[r] & CH_3I + 2H = CH_4 + HI \arrow[d] \\
& \begin{matrix}CH_3\\CH_3\end{matrix}{>}Zn + \begin{matrix}HOH\\HOH\end{matrix} = \begin{matrix}CH_4\\CH_4\end{matrix} + Zn{<}\begin{matrix}OH\\OH\end{matrix}
\end{tikzcd}$$

Zinc methyl.

(5) Instead of using zinc methyl, it is more convenient to decompose an ether solution of methyl magnesium iodide with water:

$$CH_3MgI + H_2O = CH_4 + MgI{\cdot}OH.$$

In the laboratory methane is made (6) by heating sodium acetate with soda-lime, of which the active ingredient is sodium hydroxide. The addition of the lime is for the purpose of protecting the glass vessel from the corroding action of the molten sodium hydroxide:

$$CH_3{\cdot}CO_2Na + NaOH = CH_4 + Na_2CO_3.$$

Properties.—Methane is a colourless gas possessing a slightly alliaceous odour. Its critical temperature is − 82°, and its critical pressure 45·6 atm. At low temperatures it forms colourless needles, which melt at − 184°. The boiling point under atmospheric pressure is − 164°. It is slightly soluble in water, but more readily in alcohol.

It burns with a faintly luminous, yellowish flame, and forms explosive mixtures with air, oxygen, and chlorine :

$$\underset{1\text{ vol.}}{CH_4} + \underset{2\text{ vols.}}{2O_2} = \underset{1\text{ vol.}}{CO_2} + \underset{2\text{ vols.}}{2H_2O} \text{ (steam).}$$

It is decomposed into carbon and hydrogen by the continued passage of the electric spark.

Formaldehyde is obtained from methane by the action of ozonized oxygen at ordinary temperatures. (This reaction can be used for the estimation of methane in gaseous mixtures, Ber. 45, 3515.) The partial oxidation of methane by leading a mixture of methane and air over vanadium pentoxide at 300° also yields formaldehyde (C. 1921, III. 1318). When mixed with two volumes of chlorine it explodes in direct sunlight, with separation of carbon,

$$CH_4 + 2Cl_2 = C + 4HCl.$$

In diffused sunlight chlorine substitution products are produced :

$CH_4 + Cl_2 = HCl + CH_3Cl$—Monochloromethane or methyl chloride.
$CH_3Cl + Cl_2 = HCl + CH_2Cl_2$—Dichloromethane or methylene chloride.
$CH_2Cl_2 + Cl_2 = HCl + CHCl_3$—Trichloromethane or chloroform.
$CHCl_3 + Cl_2 = HCl + CCl_4$—Tetrachloromethane or carbon tetrachloride.

Through methyl chloride methane may be converted into methyl alcohol, ethane, ethyl alcohol, and acetic acid.

Fluorine reacts explosively at − 187°.

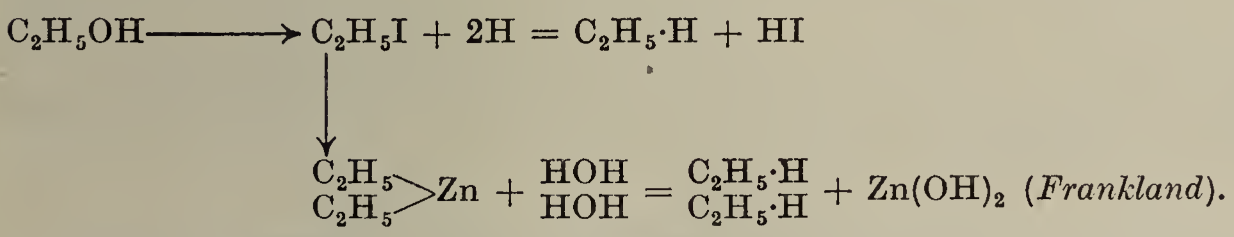
Ethane, *Ethyl hydride, Dimethyl,* $CH_3{\cdot}CH_3$, was discovered in 1848 by *Frankland* and *Kolbe.*

It is formed by the following reactions :

(1) *From the unsaturated hydrocarbons,* acetylene and ethylene, by the addition of hydrogen, whereby the double or triple link is broken down :

$$\begin{aligned} C_2H_2 + 2H_2 &= C_2H_6 \\ C_2H_4 + H_2 &= C_2H_6. \end{aligned}$$

(2) *From the corresponding alcohol,* ethyl alcohol, by way of (*a*) ethyl iodide or (*b*) of zinc ethyl, just as methane was prepared from methyl alcohol :



$$\begin{tikzcd} C_2H_5OH \arrow[r] & C_2H_5I \arrow[d] + 2H = C_2H_5{\cdot}H + HI \\ & \begin{matrix}C_2H_5\\C_2H_5\end{matrix}{>}Zn + \begin{matrix}HOH\\HOH\end{matrix} = \begin{matrix}C_2H_5{\cdot}H\\C_2H_5{\cdot}H\end{matrix} + Zn(OH)_2 \text{ (Frankland).} \end{tikzcd}$$

Or (*c*) magnesium ethyl bromide may be decomposed by water ; or (*d*) mercury ethyl by concentrated sulphuric acid :

$$\begin{aligned} C_2H_5MgBr + H_2O &= C_2H_6 + MgBr{\cdot}OH \\ (C_2H_5)_2Hg + H_2SO_4 &= 2C_2H_5{\cdot}H + HgSO_4 \text{ (Schorlemmer).} \end{aligned}$$

(3) *From Compounds derived from Methane.*—These last three methods led to the assumption that ethane was *ethyl hydride.* The following reactions show how ethane can be formed from the union of two methyl residues, and hence led to the view that the hydrocarbon was *dimethyl.* (*a*) Sodium is allowed to act on methyl iodide

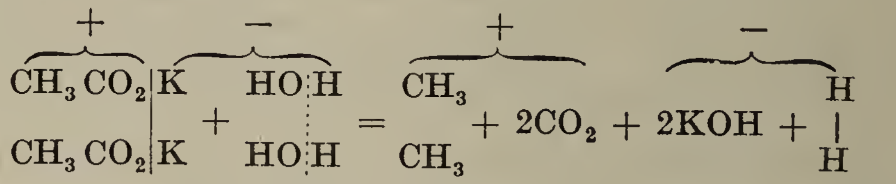
—the reaction is accelerated by the addition of one drop of acetonitrile (C. 1901, II. 24)—or (*b*) zinc methyl may be substituted for the metal :

$$2CH_3I + 2Na = CH_3 - CH_3 + 2NaI \ (\textit{Würtz}).$$
$$2CH_3I + (CH_3)_2Zn = 2CH_3 - CH_3 + ZnI_2.$$

(4) By heating acetic anhydride with barium peroxide. Acetyl peroxide is the first product, which then breaks down into ethane and CO_2 (*Schützenberger*, 1868).

$$2(CH_3CO)_2O + BaO_3 \longrightarrow C_2H_6 + (CH_3CO{\cdot}O)_2Ba + 2CO_2$$

From a theoretical point of view (5) the electrolysis of a concentrated solution of potassium acetate (p. 84) (the method used by *Kolbe* (1848) by which he discovered ethane), is of great importance. The salt breaks down into its two electrochemical constituents—potassium, its electro-positive ion, appearing at the negative pole and separating hydrogen from water at that point, and the unstable electro-negative ion radical $CH_3{\cdot}CO_2$—, which decomposes at the positive pole into $—CH_3$ and CO_2. Two methyl groups then unite to dimethyl, just as two hydrogen atoms combine to form a molecule of that element.



$$\begin{array}{l} \overbrace{CH_3CO_2}^{+}|\overbrace{K \quad HO{:}H}^{-} \quad \overbrace{CH_3 \qquad\qquad}^{+} \qquad\qquad \overbrace{\qquad\qquad H}^{-} \\ \qquad\qquad\ | \quad + \quad\ \vdots \quad = \qquad + 2CO_2 + 2KOH + | \\ CH_3CO_2|K \quad HO{:}H \quad CH_3 \qquad\qquad\qquad\qquad\qquad H \end{array}$$

It has been suggested that the *Kolbe* synthesis proceeds via the intermediate formation of acetyl peroxide, $(CH_3CO{\cdot}O)_2$, which then breaks down into C_2H_6 and $2CO_2$. The recent experiments of Walker (J.C.S. **1928**, 2040) on the breakdown of acetyl peroxide do not support this view. He was unable to obtain large yields of ethane by the thermal decomposition of acetyl peroxide, but always obtained a large amount of methane, which is not, in fact, produced by the electrolysis of potassium acetate.

Both *Kolbe* and *Frankland* believed that ethyl hydride $C_2H_5{\cdot}H$ differed from dimethyl $CH_3{\cdot}CH_3$. Such a difference was not possible in the light of the valence theory. By converting the hydrocarbon from $(C_2H_5)_2Hg$ and that obtained in the electrolysis of potassium acetate into the same ethyl chloride Schorlemmer (1863) proved the identity of ethyl hydride $C_2H_5{\cdot}H$ and dimethyl $CH_3{\cdot}CH_3$.

$$(C_2H_5)_2Hg \xrightarrow{\quad H_2SO_4 \quad} C_2H_5{\cdot}H \xrightarrow{\qquad Cl_2 \qquad} C_2H_5Cl.$$
$$2CH_3{\cdot}CO_2K \xrightarrow{\text{electric current}} CH_3{\cdot}CH_3 \xrightarrow{\qquad Cl_2 \qquad} CH_3CH_2Cl.$$

Properties.—Ethane is a colourless and odourless gas. Its critical temperature is + 34° and its critical pressure 50·2 atmospheres. It melts at − 172° and boils at − 84° under 760 mm. Its general behaviour resembles that of methane.

Homologues of Methane and Ethane

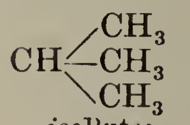
Nomenclature and Isomerism.—In consequence of the equivalence of the four valencies of carbon, no isomers are possible for the first three members of the series C_nH_{2n+2} :

CH_4	$CH_3—CH_3$	$CH_3—CH_2—CH_3.$
Methane.	Ethane.	Propane.

Two structural isomers exist for the fourth member, C_4H_{10} :

$CH_3—CH_2—CH_2—CH_3$
Normal Butane.

and



$$CH\begin{cases}CH_3\\CH_3\\CH_3\end{cases}$$

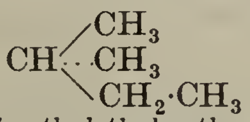
*iso*Butane.

In the name trimethylmethane for *iso*butane, isomeric with normal butane, it is indicated that this substance is derived from methane by the replacement of three hydrogen atoms by three methyl groups.

For the fifth member, pentane, C_5H_{12}, three isomers are possible :

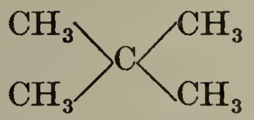
$$CH_3—CH_2—CH_2—CH_2—CH_3$$

Normal Pentane.



Dimethylethylmethane.

and



Tetramethylmethane.

The number of theoretically possible isomers now increases rapidly. Hexane, C_6H_{14}, has 6 isomers ; heptane, C_7H_{16}, 9 isomers ; octane, C_8H_{18}, 18 isomers ; tridecane, $C_{13}H_{28}$, 802 isomers. On the calculation of the number and nature of the isomeric paraffins, see Chem. Ztg. 1898, I. 395.

Commencing with the fifth member, the names are formed from the Greek words representing numbers.

Formation.—In preparing the homologous paraffins, the homologues of ethyl alcohol $C_nH_{2n+1}·OH$ and the saturated fatty acids are employed.

I. *Formation from compounds containing the same number of carbon atoms*

(1) From the unsaturated hydrocarbons by the addition of hydrogen (see Ethane).

(2) By the reduction of alcohols, ketones, and carboxylic acids.

(*a*) The alcohol, for example ethyl alcohol, is changed to the chloride, bromide, or iodide, which is then reduced with nascent hydrogen, by means of zinc and hydrochloric acid, or sodium amalgam and alcohol. The iodide may alternatively be treated with aluminium chloride (Ber. **27**, 2766).

Thus, propane has been prepared from the two propyl iodides C_3H_7I by zinc and hydrochloric acid, as well as from *iso*propyl chloride by sodium-ammonium (C. 1905, II. 112). By heating the alkyl iodides with zinc and water in sealed tubes at 120–180°, paraffins are obtained.

(*b*) The saturated fatty acids, $C_nH_{2n+1}·CO_2H$, particularly the higher members of the series, may be reduced to the corresponding paraffins by heating them with concentrated hydriodic acid and red phosphorus to 200–250° :

$$\underset{\text{Stearic acid.}}{C_{17}H_{37}·CO_2H} + 6HI = \underset{\text{Octadecane.}}{C_{18}H_{38}} + 3I_2 + 2H_2O.$$

(*c*) The ketones (*q.v.*), resulting from the distillation of the calcium salts of fatty acids, are reduced to paraffins when they are heated with hydriodic acid. It is more practical first to prepare the keto-chlorides by the action of phosphorus pentachloride upon the ketones, and then to reduce them.

The last two reactions especially were applied (Ber. **15**, 1687, 1711 : **19**, 2218) in the preparation of the normal hydrocarbons from nonane, $CH_3(CH_2)_7CH_3$, to tetracosane, $CH_3(CH_2)_{22}CH_3$.

Acetoacetic ester and its mono- and dialkyl substitution products yield paraffins on electrolytic reduction in sulphuric acid solution ; changes in the carbon skeleton may, however, take place during the reduction (Ber. **45**, 437).

(3) *From Organometallic Compounds.*—The alcohol is changed by way of the alkyl iodide into a zinc or mercury alkyl, and the zinc alkyls are then decomposed by water (see Methane and Ethane),

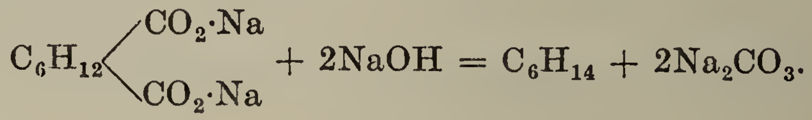
and the mercury alkyls by acids (see Ethane). Also, the easily prepared magnesium halogen alkyls may be decomposed by water, thereby liberating the paraffin (C. 1901, I. 1000).

II. *Formation from compounds containing a greater number of carbon atoms*

(4) A mixture of the salts of fatty acids and an alkali hydroxide, or better, soda-lime, is subjected to dry distillation.

$$^{*}\,R{\cdot}COONa + NaOH = Na_2CO_3 + R{\cdot}H.$$

When the higher fatty acids are subjected to this treatment, the usual products are the ketones. Hydrocarbons are, however, produced when sodium methoxide is used in place of soda-lime (Ber. **22**, 2133). The dibasic acids are similarly decomposed:



$$C_6H_{12}\begin{cases}CO_2{\cdot}Na\\CO_2{\cdot}Na\end{cases} + 2NaOH = C_6H_{14} + 2Na_2CO_3.$$

III. *Formation by joining two alkyl groups together*

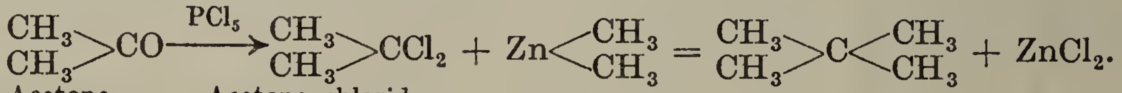
(5) *Method of Wurtz*: this consists in the action of sodium (or reduced silver or copper) on the bromides or iodides of the alcohol radicals in ethereal solution (see Ethane). Thus with sodium:

C_2H_5I	yields	$C_2H_5{\cdot}C_2H_5$	Diethyl or normal Butane.
$CH_3CH_2CH_2I$	,,	$C_3H_7{\cdot}C_3H_7$	Di-propyl or normal Hexane.
$CH_3CH_2CH_2CH_2I$	,,	$C_4H_9{\cdot}C_4H_9$	Di-butyl or normal Octane.

The addition of one or two drops of acetonitrile accelerates the reaction (C. 1901, II. 24). This reaction proceeds especially easily with normal alkyl iodides of high molecular weights. Thus, *Hell* and *Hägele*, by fusing myricyl iodide with sodium, obtained hexacontane, $C_{60}H_{122}$, a compound having the longest normal carbon chain known up to the present time (Ber. **22**, 502). By employing a mixture of the iodides of two primary alcohols, a mixture of hydrocarbons results, *e.g.* a mixture of R·I and R′·I gives with sodium a mixture of the hydrocarbons RR, RR′, and R′R′. The iodides of optically active alcohols, *e.g.* optically active amyl iodide, yield optically active paraffins. Magnesium acts similarly to sodium on the iodides of the higher alcoholic radicals (C. 1901, I. 999: Ber. **36**, 3083), for example: tertiary butyl bromide and magnesium give hexamethylethane $(CH_3)_3C{\cdot}C(CH_3)_3$, which is also formed by the interaction of pentamethylethyl bromide and methyl magnesium bromide (C. 1906, II. 748):

$$C(CH_3)_3{\cdot}C(CH_3)_2Br + CH_3MgBr = (CH_3)_3C{\cdot}C(CH_3)_3 + MgBr_2.$$

(6) Action of zinc alkyls on alkyl halides and ketone chlorides: thus, tertiary butyl iodide and zinc ethyl give trimethylethylmethane (Ber. **32**, 1445: **33**, 1905); β-dichloropropane is changed by zinc methyl into tetramethylmethane:



$$\begin{matrix}CH_3\\CH_3\end{matrix}{>}CO \xrightarrow{PCl_5} \begin{matrix}CH_3\\CH_3\end{matrix}{>}CCl_2 + Zn{<}\begin{matrix}CH_3\\CH_3\end{matrix} = \begin{matrix}CH_3\\CH_3\end{matrix}{>}C{<}\begin{matrix}CH_3\\CH_3\end{matrix} + ZnCl_2.$$

Acetone. Acetone chloride.

The alkylmagnesium halides also react with alkyl halides, but less readily than the zinc alkyls, with the formation of paraffins (Ber. **37**, 488).

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* R is a general abbreviation for an alkyl group, and means CH_3, C_2H_5, C_3H_7, or, in general, a group C_nH_{2n+1}. The abbreviations Me, Et are frequently used for the methyl and ethyl groups and Ac for the acetyl group, $CH_3{\cdot}CO-$. These abbreviations will be used in this book where convenient.

(7) By the electrolysis of the alkali salts of fatty acids (see Ethane). Alcohols may occur as subsidiary products: methyl alcohol from potassium acetate; ethyl alcohol from sodium propionate. Also unsaturated hydrocarbons, as *iso*butylene, are produced from trimethylacetic acid.

Synthetic Methods.—The last group of reactions comprises synthetic methods for the building up of hydrocarbons. In the formation of methane from carbon disulphide and hydrogen sulphide it was explained what in general was understood by the synthesis of a carbon compound. Those reactions in which carbon atoms, not before combined with one another, become united, claim particular importance in the synthesis of the compounds of carbon (*Lieben*, Ann. **146,** 200). Such reactions are the synthetic methods of organic chemistry in the more restricted sense, and may be called *nuclear syntheses.*

The synthesis of a carbon compound from derivatives of known structure is one of the most important means employed for the recognition of its structure or constitution.

Properties of the Paraffins.—The lowest members of the series up to butane and tetramethyl methane are gases at the ordinary temperature. The middle members are colourless liquids, with a faint but characteristic odour. The higher representatives, beginning with hexadecane, $C_{16}H_{34}$, m.p. 18°, are crystalline solids. The highest members are only volatile without decomposition under reduced pressure. The boiling points rise with the molecular weights; the difference for CH_2 is at first 30°, and with the higher members it varies from 25° to 13°.

The boiling points of propane, of the two butanes, the three pentanes, and the five known hexanes are given in the following table. All the theoretically possible isomers are known:

	Name.	Structural Formula.	B.P. at 760 mm.
C_3H_8	**Propane**	$CH_3{\cdot}CH_2{\cdot}CH_3$	− 45°
C_4H_{10}	**Butanes**		
	Normal Butane	$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3$	+ 1°
	*iso*Butane (Trimethylmethane)	$CH_3{\cdot}CH(CH_3)_2$	− 11·5°
C_5H_{12}	**Pentanes**		
	Normal Pentane . . .	$CH_3{\cdot}[CH_2]_3{\cdot}CH_3$	+ 38°
	*iso*Pentane (Dimethylethylmethane)	$(CH_3)_2CH{\cdot}C_2H_5$	+ 30°
	Tetramethylmethane . .	$C(CH_3)_4$	+ 9°
C_6H_{14}	**Hexanes**		
	Normal Hexane . . .	$CH_3[CH_2]_4CH_3$	+ 71°
	*iso*Hexane (Dimethylpropylmethane)	$(CH_3)_2CH{\cdot}[CH_2]_2CH_3$	+ 62°
	Methyldiethylmethane . .	$CH_3CH(C_2H_5)_2$	+ 64°
	Di*iso*propyl	$(CH_3)_2CH{\cdot}CH(CH_3)_2$	+ 58°
	Trimethylethylmethane .	$(CH_3)_3C{\cdot}C_2H_5$	+ 49°

It is evident from this table that among isomers those with normal structure (p. 35) have the highest boiling points: generally the accumulation of methyl groups in the molecule lowers the boiling points. The same regularity will be again encountered in other homologous series.

The subjoined table contains the melting points, boiling points, and the specific gravities of the known normal paraffins:

		M.P.		B.P.	Sp. Gr.	
Heptane	C_7H_{16}	. . .	Under 760 mm. pressure.	98·4°	0·7006 (0°)	
Octane	C_8H_{18}	. . .		125·5°	0·7188 (0°)	
Nonane	C_9H_{20}	− 51°		149·5°	0·7330 (0°)	
Decane	$C_{10}H_{22}$	− 32°		173°	0·7456 (0°)	
Undecane	$C_{11}H_{24}$	− 26·5°		194·5°	0·7745	at their m.p.
Dodecane	$C_{12}H_{26}$	− 12°		214°	0·773	
Tridecane	$C_{13}H_{28}$	− 6·2°		234°	0·775	
Tetradecane	$C_{14}H_{30}$	+ 5·5°		252·5°	0·775	
Pentadecane	$C_{15}H_{32}$	+ 10°		270·5°	0·775	
Hexadecane	$C_{16}H_{34}$	+ 18°		287·5°	0·775	
Heptadecane	$C_{17}H_{36}$	+ 22·5°		303°	0·776	
Octadecane	$C_{18}H_{38}$	+ 28°		317°	0·776	
Nonadecane	$C_{19}H_{40}$	+ 32°		330°	0·777	
Eicosane	$C_{20}H_{42}$	+ 36·7°	Under 15 mm. pressure.	205°	0·777	
Heneicosane	$C_{21}H_{44}$	+ 40·4°		215°	0·778	
Docosane	$C_{22}H_{46}$	+ 44·4°		224·5°	0·778	
Tricosane	$C_{23}H_{48}$	+ 47·7°		234°	0·778	
Tetracosane	$C_{24}H_{50}$	+ 51·1°		243°	0·778	
Heptacosane	$C_{27}H_{56}$	+ 59·5°		270°	0·779	
Nonocosane	$C_{29}H_{60}$	+ 62·7°				
Hentriacontane	$C_{31}H_{64}$	+ 68·1°		302°	0·780	
Dotriacontane	$C_{32}H_{66}$	+ 70·0°		310°	0·781	
Pentatriacontane	$C_{35}H_{72}$	+ 74·7°		331°	0·781	
Hexacontane	$C_{60}H_{122}$	+ 102°		. . .	. . .	

n-Heptane is formed during the distillation of the resin of *Pinus Sabiniana* and *Pinus Jeffreyi* (C. 1901, I. 1143). *Methylethylpropylmethane,* one of the isomers of *n*-heptane, is the simplest hydrocarbon containing an asymmetric C-atom (see p. 38). Its *dextro-rotatory* form, b.p. 91°, and $[\alpha]_D = +9{\cdot}5°$, is prepared by the action of sodium on a mixture of ethyl iodide and *d*-amyl iodide (Ber. **37**, 1046).

A large number of isomeric octanes and nonanes have been prepared (J.A.C.S. **33**, 520 : **34**, 680).

Of the isomers of *n*-octane, *hexamethylethane* $(CH_3)_3C{\cdot}C(CH_3)_3$, m.p. 104°, b.p. 107°, should be mentioned on account of its high vapour pressure, and similarity to perchlorethane (p. 122); it results from the reaction of pentamethyl ethyl bromide and methyl magnesium bromide (C. 1906, II. 748).

Heptacosane and hentriacontane have been found in American tobacco (C. 1901, II. 395).

n-*Nonocosane* has been obtained from cabbage fat (Biochem. J. **23**, 168).

The saturated hydrocarbons are insoluble in water, whilst the lower and intermediate members are readily soluble in alcohol and ether. The solubility in these last two solvents falls with increasing molecular weight: dimyricyl, $C_{60}H_{122}$, m.p. 102°, is scarcely soluble in either of them.

The specific gravities of the liquid and solid hydrocarbons increase with their molecular weights, but are always less than that of water. It is remarkable that in the case of the higher members the specific gravities at the point of fusion are almost the same. They rise from 0·773 for dodecane, $C_{12}H_{26}$, to but 0·781 for pentatriacontane, $C_{35}H_{72}$; consequently the molecular volumes are nearly proportional to the molecular weights (Ber. **15**, 1719 : Ann. **223**, 268).

The paraffins are not absorbed by bromine in the cold or sulphuric acid, being in this way readily distinguished and separated from the unsaturated hydrocarbons. They are very stable, and, in consequence, react with difficulty. Fuming nitric acid and even chromic acid are without much effect upon them in the cold; when heated, however, they generally are oxidized directly to carbon dioxide and water. Recently, *n*-hexane and *n*-octane have been nitrated by heating them with dilute nitric acid. The isomers are more easily attacked than are the normal paraffins. When acted on by chlorine or bromine they yield substitution products.

When paraffins are nitrated or chlorinated, in general the hydrogen attached to a tertiary carbon atom is replaced rather than that attached to a secondary, and the latter rather than that attached to a primary carbon atom.

When oxidized in a current of air at 100°, paraffin-wax yields a mixture of fatty acids and non-acidic compounds, from which the isolation of individual substances is nearly impossible. By the oxidation of pure *n*-triacontane, it has been shown that the first product is probably a secondary alcohol, which is then oxidized to a ketone, and this to the acids. Oxidation probably starts at the fourth carbon atom of the chain, and the product with the longest chain which was isolated was one containing 26 carbon atoms (Francis and Wood, J.C.S. **1927,** 1897).

Technical Production of the Saturated Hydrocarbons.—The hydrocarbons, readily obtainable on a commercial scale, are employed in enormous quantities for illuminating and heating purposes, are also used as solvents for fats, oils, and resins, as lubricants for machinery, and as salves.

The great abundance of mineral oil, petroleum, rock-oil, naphtha, is of the utmost importance to chemical industry. The oil is very widely distributed, but only occurs in certain districts in sufficiently large quantities to be usefully worked. It is especially abundant in Pennsylvania and Canada, although it is also found in the Crimea along the Black Sea, and at Baku on the shore of the Caspian, as well as in Hungary, Galicia, Roumania, and the Argentine Republic. Its occurrence in Germany, in Hanover, and in Alsace is limited. Since the year 1859 efforts have been put forth to work oil wells which have been known for many years, and also to make new borings. (See *C. Engler* and *H. Höfer*, Das Erdöl, Hirzel, 1913.)

In 1925 the world-production of crude oil was some 147 million tons: of this America produced 103, Russia 7·4, Galicia 0·8 and Roumania 2·3 millions.

In a crude state it is a thick, oily liquid, of brownish colour, which appears green by reflected light. Its more volatile constituents are lost upon exposure to the air; it then thickens and eventually passes into asphaltum. The greatest differences prevail in the various kinds of petroleum. It is very probable that petroleum has been produced by the decomposition of the fatty constituents of fossil animals. This took place under the influence of great pressure and the heat of the earth. The distillation of fish blubber under pressure has yielded products very similar to American petroleum (*Engler*, Ber. **26,** 1449: **30,** 2908: **33,** 7: *Ochsenius*, Ber, **24,** R. 594).

By distillation with kieselguhr or aluminium chloride, cholesterol yields a similar mixture of hydrocarbons, which, like natural petroleum, is optically active (*Steinkopf*, J. pr. Chem. **100,** 65: *Zelinsky*, Ber. **60,** 1793).

Mendelejeff first suggested that it was possible for petroleum to be formed by the action of water on the metallic carbides in the interior of the earth, and *Moissan* subsequently came to the same conclusion during his investigations on the carbides (Ber. **29**, R. 614).

Apart from geological evidence the following facts contradict this view and favour an organic origin for petroleum: (1) a small nitrogen content (pyridine bases) in most specimens of petroleum; (2) the optical activity of the higher fractions, which according to present knowledge could not be formed by such a synthesis, as this would lead to the formation of racemic (inactive) bodies only.

A short review of the theories of the origin of petroleum is given in Naturwissenschaften, **1925**, 623.

The constituents of American petroleum possessing a low boiling point, consist almost entirely of saturated hydrocarbons, both normal paraffins and those of the general formulæ $R_2\cdot CH\cdot CH\cdot R_2$, CHR_3, and CR_4 (Ber. **32**, 1445: **33**, 1905). Small quantities of some of the aromatic hydrocarbons (cumene and mesitylene) are present. The crude oil has a specific gravity of 0·8–0·92, and distils from 30° to 360° and higher. Various products, of technical value, have been obtained from it by fractional distillation: *Petroleum spirit*, sp. gr. 0·665–0·67, distilling about 50°–60°, consists of pentane and hexane; *petroleum benzine*, sp. gr. 0·68–0·72 (not to be confounded with the benzene of coal tar), distils at 70–90°, and is composed of hexane and heptane; *ligroin*, boiling from 90° to 120°, consists principally of heptane and octane; *refined petroleum*, called also kerosene, boils from 150° to 300°, sp. gr. 0·78–0·82. The portions boiling at high temperatures are applied as lubricants; small amounts of *vaseline* and *paraffin* (see below) are obtained from them.

Caucasian petroleum (from Baku) has a higher specific gravity than the American; it contains far less of the light volatile constituents, and distils at about 150°. Upwards of 10 per cent. of benzene hydrocarbons (C_6H_6 to cymene $C_{10}H_{14}$) as well as less saturated hydrocarbons, C_nH_{2n-8}, etc., may be extracted by shaking it with concentrated sulphuric acid (Ber. **19**, R. 672). These latter are also present in the German oils (Naphthenes, Ber. **20**, 595). That portion of the Caucasian petroleum insoluble in sulphuric acid consists almost exclusively of C_nH_{2n} hydrocarbons, the naphthenes, which belong to the *cyclo*paraffins (Vol. II) and are probably chiefly *cyclo*pentanes, mixed with hydrogenated aromatic compounds. From its composition, Galician petroleum occupies a position between American petroleum and that from Baku.

German petroleum also contains benzene hydrocarbons (extractable by sulphuric acid), but consists chiefly of the saturated hydrocarbons and naphthenes (*Krämer*, Ber. **20**, 595). The so-called petrolic acids are present in all varieties of petroleum, particularly that from Russia.

Products similar to those occurring in mineral oil are yielded by the tars resulting from the dry distillation of brown-coal (from the province of Saxony), and of the bituminous shale (in Scotland and the Gewerkschaft Messel, Darmstadt, in Hesse). These tars contain appreciably greater quantities of unsaturated hydrocarbons associated with the naphthenes and paraffins, as well as the aromatic hydrocarbons present in the tar from bituminous shales (*Heusler*, Ber. **28**, 488: **30**, 2743: Z. anorg. Chem. 1896, 319). Large quantities of solid paraffins are also present in these tar oils, from which up to 46 per cent. of lower boiling hydrocarbons can be obtained by destructive distillation at 350° to 500°. A mixture of paraffin hydrocarbons can be obtained from "low-temperature tar," obtained by carbonization of coal at 350–500° (*Pictet, Fischer*, and others, Ber. **46**, 3342: **52**, 1035, 1053).

By *solid paraffin* is ordinarily understood the high-boiling solid hydrocarbons (above 300°) obtained by the distillation of the tar of wood, peat, lignite, and bituminous shales. They were discovered by Reichenbach (1830) in the tar from the beech-wood, and in nature occur more abundantly in the petroleum from Baku than in that from America. In the free state they constitute the class of mineral waxes, which includes *ozokerite* (in Galicia and Roumania, and Tscheleken, an island in the Caspian Sea, Ber. **16**, 1547); and *neftigil* (in Baku). For their purification the crude paraffins are treated with concentrated sulphuric acid, to destroy the resinous constituents, and are then re-distilled. Ozokerite that has been bleached without distillation, bears the name *ceresine*, and is used as a substitute for beeswax. Paraffins that liquefy readily and fuse between 30° and 40° are known as *vaselines*, and find application as salves.

When pure, the solid paraffins form a white, translucent, leafy, crystalline mass, soluble in ether and hot alcohol. They melt between 45° and 70°, and are essentially a mixture of saturated hydrocarbons boiling above 300°, but appear to contain also those of the formula C_nH_{2n}. Chemically, paraffin is extremely stable, and is not attacked by fuming nitric acid. Substitution products are formed when chlorine acts upon paraffin in a molten state.

B. UNSATURATED HYDROCARBONS

The unsaturated hydrocarbons are those hydrocarbons containing one or more double or triple bonds in the molecule, and will be discussed here in the following classes:

1. Hydrocarbons C_nH_{2n} : Olefines.
2. Hydrocarbons C_nH_{2n-2} : Acetylenes.
3. Hydrocarbons C_nH_{2n-2} : Diolefines.
4. Hydrocarbons C_nH_{2n-4}.
5. Hydrocarbons C_nH_{2n-6}.
6. Still more unsaturated hydrocarbons.

1. OLEFINES OR ALKYLENES, C_nH_{2n}

The hydrocarbons of this series contain two hydrogen atoms less than the saturated hydrocarbons. All contain two adjacent carbon atoms united doubly to each other, or, as commonly expressed, they contain a double carbon linkage. The olefines readily take up two univalent atoms or radicals, whereby the double carbon union becomes converted into a single one: paraffins or their derivatives result.

The names of the olefines are derived from the names of the alcohols containing a like carbon content, with the addition of the suffix "ene": ethylene from ethyl, propylene from propyl, and finally for the series we have the name: alkylenes. In the "Geneva names" the *yl* of the alcohol radicals is replaced by "ene": [ethene] from ethyl, [propene] from propyl, and for the series: alkenes. In long series the position of the double union is indicated by an added number or Greek letter. Methylene, $=CH_2$, the hydrogen compound corresponding to CO, has thus far resisted isolation. Two $=CH_2$ groups invariably unite to form ethylene—the first member of the series. Beginning with the second member of the series, propylene, we find, as we advance, that the olefines have isomers in the ring-compounds—the *cyclo*paraffins.

Propylene is isomeric with *cyclo*propane, $\begin{array}{l}CH_2\\CH_2\end{array}\!\!>CH_2$.

The three butylenes are isomeric with *cyclo*butane, $\begin{array}{l}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{array}$

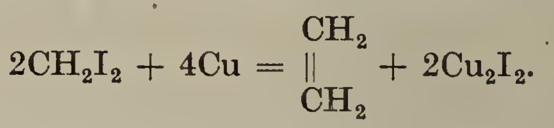
The amylenes and hexylenes are similarly isomeric with *cyclo*pentane and *cyclo*hexane.

The *cyclo*paraffins are more closely allied in chemical character to the paraffins than to the isomeric olefines. They do not show the great additive power of the latter, as addition would necessitate a rupture of the ring. They will be discussed in a subsequent volume with other ring compounds.

Ethylene may be taken as being typical of the olefines.

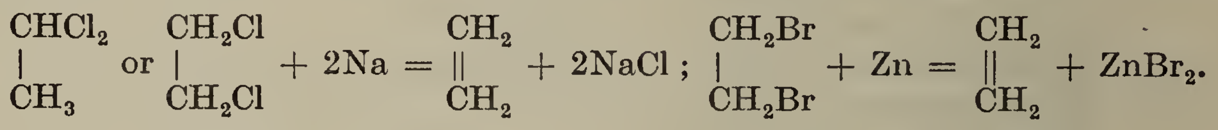
Ethylene, $CH_2{=}CH_2$ [*Ethene*], *Elayl*, is also known as *olefiant gas*, because, by the action of chlorine, it yields an oily compound, ethylene chloride (*q.v.*). This property has given the name to the whole series. Ethylene is formed during the dry distillation of many organic bodies, and is present in illuminating gas to the extent of 4 to 5 per cent.

Methods of Formation.—(1) By heating methylene iodide, CH_2I_2, with metallic copper to 100° in a sealed tube (*Butlerow*):



$$2CH_2I_2 + 4Cu = \begin{array}{c}CH_2\\ \|\\ CH_2\end{array} + 2Cu_2I_2.$$

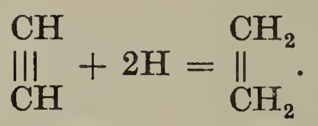
(2) By the action of metallic sodium on ethylidene chloride (*Tollens*) and ethylene chloride, as well as from zinc and ethylene bromide:



$$\begin{array}{l}CHCl_2\\ |\\ CH_3\end{array} \text{ or } \begin{array}{l}CH_2Cl\\ |\\ CH_2Cl\end{array} + 2Na = \begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + 2NaCl;\ \begin{array}{l}CH_2Br\\ |\\ CH_2Br\end{array} + Zn = \begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + ZnBr_2.$$

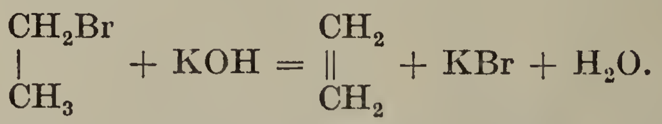
A convenient laboratory method for the preparation of pure ethylene is the action of the zinc-copper couple on an alcoholic solution of ethylene bromide.

(3) By the action of zinc and ammonia on copper acetylide, or by hydrogenation of acetylene in presence of finely divided metals such as nickel.



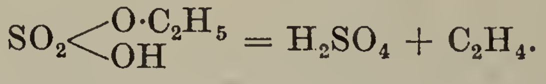
$$\begin{array}{l}CH\\ |||\\ CH\end{array} + 2H = \begin{array}{l}CH_2\\ \|\\ CH_2\end{array}.$$

(4) By the action of alcoholic potassium hydroxide on ethyl bromide:



$$\begin{array}{l}CH_2Br\\ |\\ CH_3\end{array} + KOH = \begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + KBr + H_2O.$$

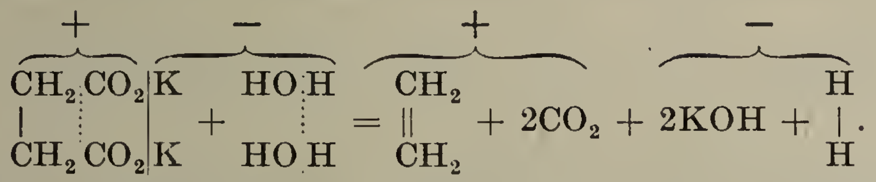
(5) Upon heating ethyl sulphuric acid (p. 168). This is the method usually pursued in the laboratory for the preparation of ethylene (Ann. **192**, 244):



$$SO_2\!<\!\begin{array}{l}O\cdot C_2H_5\\OH\end{array} = H_2SO_4 + C_2H_4.$$

Sulphuric acid may be replaced, with advantage, by syrupy phosphoric acid, because no charring occurs when this acid is employed. The ethylene is evolved when alcohol is slowly dropped into the acid which is heated to 200–220° (C. 1901, II. 177).

(6) By the electrolysis of a concentrated solution of potassium succinate (see Ethane) (*Kekulé*):



$$\overbrace{\begin{array}{l}CH_2\cdot CO_2\\ |\\ CH_2\cdot CO_2\end{array}}^{+}\Bigg|\overbrace{\begin{array}{l}K\\ \\ K\end{array} + \begin{array}{l}HO\cdot H\\ \vdots\\ HO\cdot H\end{array}}^{-} = \overbrace{\begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + 2CO_2}^{+} + \overbrace{2KOH + \begin{array}{c}H\\ |\\ H\end{array}}^{-}.$$

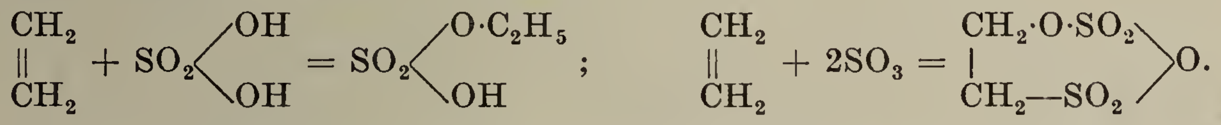
Properties.—Ethylene is a colourless gas, with a peculiar, sweetish odour: it is now sometimes used as an anæsthetic. Water dissolves but small quantities of it, whilst alcohol and ether absorb about 2 volumes. It is liquefied at 0°, at a pressure of 42 atmospheres. Its critical temperature is 13°, and its critical pressure exceeds 60 atmospheres. It melts at — 169° and boils under atmospheric pressure at — 105°. It can be used for the production of very low temperatures (Ber. **32**, 49). It burns with a bright, luminous flame, decomposing initially into methane and acetylene (Ber. **27**, R. 459). A mixture of ethylene and chlorine when ignited burns slowly with a very sooty flame. It forms a strongly explosive mixture with oxygen (3 volumes).

Reactions.—(1) In the presence of platinum black, it will combine with hydrogen at ordinary temperatures, yielding C_2H_6 (Ber. **7**, 354).

(2) It is absorbed by concentrated hydrobromic and hydriodic acids at 100°, with the production of C_2H_5Br and C_2H_5I:

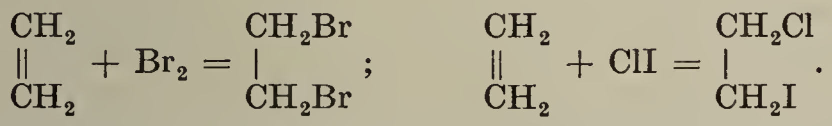
$$\begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + H_2 = \begin{array}{l}CH_3\\ |\\ CH_3\end{array};\qquad \begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + HI = \begin{array}{l}CH_2I\\ |\\ CH_3\end{array}.$$

(3) It combines with sulphuric acid at 160°–174° forming ethyl hydrogen sulphate, and with sulphuric anhydride to yield carbyl sulphate. The combination of ethylene with sulphuric acid in the presence of metallic catalysts is of technical importance in the conversion of ethylene to ethyl alcohol (C. 1921, II. 265).



$$\begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + SO_2\Big\langle\begin{array}{l}OH\\ \\ OH\end{array} = SO_2\Big\langle\begin{array}{l}O\cdot C_2H_5\\ \\ OH\end{array};\qquad \begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + 2SO_3 = \begin{array}{l}CH_2\cdot O\cdot SO_2\\ |\\ CH_2{-}{-}SO_2\end{array}\Big\rangle O.$$

(4) It unites readily with chlorine and bromine, as well as with iodine in alcoholic solution, and with the two iodine chlorides (Ber. **26**, 368):

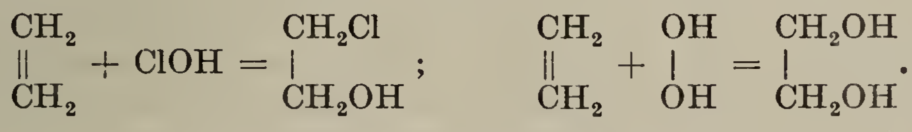


$$\begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + Br_2 = \begin{array}{l}CH_2Br\\ |\\ CH_2Br\end{array};\qquad \begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + ClI = \begin{array}{l}CH_2Cl\\ |\\ CH_2I\end{array}.$$

The reaction between ethylene and bromine is catalysed by the glass surface of the reaction vessel and does not take place if the glass is covered with paraffin: Norrish, J.C.S., **123**, 3006.

(5) It forms the monochlorhydrin of glycol by its union with hypochlorous acid.

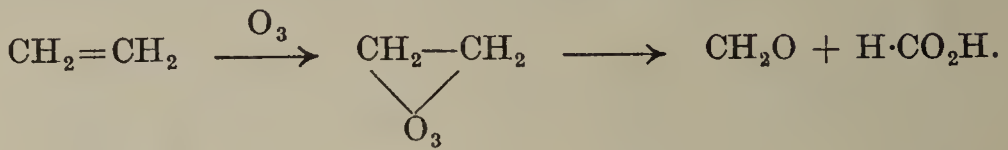
(6) Ethylene glycol itself, however, is produced by carefully oxidizing ethylene with dilute potassium permanganate, which acts as if hydrogen peroxide added itself to the ethylene:



$$\begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + ClOH = \begin{array}{l}CH_2Cl\\ |\\ CH_2OH\end{array};\qquad \begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + \begin{array}{l}OH\\ |\\ OH\end{array} = \begin{array}{l}CH_2OH\\ |\\ CH_2OH\end{array}.$$

(7) Ethylene combines with ozone to give the *ozonide*, a colour-

less, very explosive liquid, which is decomposed by water into formaldehyde and formic acid (Ber. **42**, 3305):



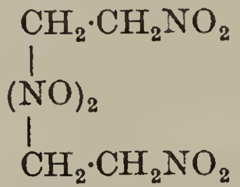
$$CH_2{=}CH_2 \xrightarrow{O_3} CH_2{-}CH_2(O_3) \longrightarrow CH_2O + H{\cdot}CO_2H.$$

The constitution of the ozonide is discussed on p. 106.

At 585° ethylene can be oxidized by atmospheric oxygen to formaldehyde in good yield (Willstätter, Ann. **422**, 36).

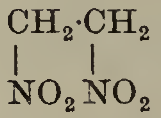
(8) By the action of nitrating acid at 0°, glycol dinitrate $C_2H_4(ONO_2)_2$ and β-nitroethyl nitrate $NO_2C_2H_4{\cdot}ONO_2$ are produced (*Wieland*, Ber. **53**, 201).

(9) Addition of N_2O_3 and NO_2 to ethylene yields a *pseudo*-nitrosite (bis-nitrosonitro compound) and a dinitro compound (*Wieland*, Ann. **424**, 72).



$$CH_2{\cdot}CH_2NO_2{-}(NO)_2{-}CH_2{\cdot}CH_2NO_2$$

*pseudo*nitrosite



$$NO_2CH_2{\cdot}CH_2NO_2$$

dinitro compound.

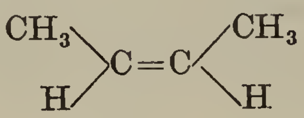
(10) Ethylene and its homologues readily form co-ordination compounds with many metallic salts such as CuCl . . . C_2H_4, H_2O (Ann. **370**, 286): C_2H_4 . . . $HgOH{\cdot}Cl$ (Ann. **420**, 170: Ber. **53**, 984): $AlCl_3{\cdot}3C_2H_4{\cdot}H_2O$ (J.A.C.S. **38**, 1384). The mercury compound is fairly stable, but the cuprous and aluminium compounds are unstable.

Ethylene Homologues.—Higher olefines are found in the tar obtained from bituminous shales (Ber. **28**, 496), in American petroleum (C. 1906, II. 120), and apparently also in coal tar (Ber. **38**, 1296).

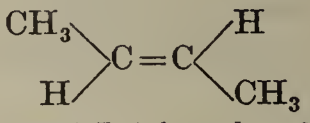
Olefine isomers appear first with butylene. Three modifications are possible and are known:

(1) $CH_3{-}CH_2{-}CH{=}CH_2$ Butylene. (2) $CH_3{-}CH{=}CH{-}CH_3$ *pseudo*Butylene. (3) $CH_2{=}C(CH_3)_2$ *iso*Butylene.

*pseudo*Butylene has been obtained in two geometrical isomeric modifications (p. 41) (Ann. **313**, 207):



*cis-pseudo*Butylene, b.p. 1–1·5°.



*trans-pseudo*Butylene, b.p. 2·5°.

Five olefines of the formula C_5H_{10} are possible.

Methods of Formation.—(1) The halogen derivatives, readily formed from the alcohols, are digested with alcoholic sodium or potassium hydroxide.

In this reaction the haloid (especially the iodide) derivatives corresponding with the secondary and tertiary alcohols break up very readily. Propylene has been obtained from *iso*propyl iodide, α-butylene from the iodide of normal butyl alcohol, β-butylene from secondary butyl iodide, and *iso*butylene from the iodide of tertiary butyl alcohol. Many others have been prepared in the same way. Heating with lead oxide effects the same result (Ber. **11**, 414). Tertiary iodides yield olefines when treated with ammonia.

(2) Distillation of the monohydric alcohols, $C_nH_{2n+1}OH$, with dehydrating agents, *e.g.* sulphuric acid, zinc chloride, and phosphorus pentoxide (C. 1901, II. 77), or boron trioxide or oxalic acid (C. 1898,

I. 557 : Ber. **34**, 3249) or passage of their vapours over heated anhydrous alumina (Ber. **36**, 1990) causes the loss of one molecule of water and the formation of the corresponding olefine. Isomeric and polymeric forms are produced together with the expected olefine.

When sulphuric acid acts on the alcohols, the alkyl hydrogen sulphates appear as intermediate products. When heated, these break down into sulphuric acid and the olefines. In many cases, however, the loss of water seems to be due to a true catalytic action of the acid (Ann. **385**, 227).

The secondary and tertiary alcohols decompose particularly readily. The higher alcohols, not volatile without decomposition, undergo the above change when heat is applied to them ; thus cetene, $C_{16}H_{32}$, is formed on distilling cetyl alcohol, $C_{16}H_{34}O$.

The higher olefines may be obtained from the corresponding alcohols by distilling the esters they form with the fatty acids. The products are an olefine and an acid (Ber. **16**, 3018) :

$$\underset{\text{Dodecyl palmitate.}}{C_{15}H_{31}CO_2C_{12}H_{25}} = \underset{\text{Palmitic acid.}}{C_{15}H_{31}CO_2H} + \underset{\text{Dodecylene.}}{C_{12}H_{24}}.$$

Also, xanthogenic esters decompose at relatively low temperatures into olefines, carbon oxysulphide and mercaptans (Ber. **32**, 3332 : **46**, 244).

(3) Halogen addition products of the olefines react with metals to form free olefines.

(4) By heating alkylammonium phosphates (Ber. **34**, 300).

(5) The electrolysis of the potassium salts of saturated dicarboxylic acids yields olefines, *e.g.* glutaric acid yields propylene (C. 1904, II. 823).

(6) By the action of zinc alkyls on the halogen derivatives of the olefines, *e.g.* zinc ethyl and bromoethylene yield butylene :

$$2CH_2 : CHBr + Zn(C_2H_5)_2 \longrightarrow CH_2 : CH{\cdot}C_2H_5.$$

(7) Higher olefines have also been obtained by the reaction of Wurtz (p. 96).

(8) The formation of higher olefines by the linking of lower members with tertiary alcohols or alkyl iodides, is noteworthy. Thus, from tertiary butyl alcohol and *iso*butylene, by means of zinc chloride or sulphuric acid, di*iso*butylene is obtained (Ann. **189**, 65 : Ber. **27**, R. 626) :

$$(CH_3)_3C{\cdot}OH + CH_2 : C(CH_3)_2 = (CH_3)_3C{\cdot}CH : C(CH_3)_2 + H_2O.$$

The action of the $ZnCl_2$ is due to the intermediate formation of addition products, *e.g.* trimethylethylene and zinc chloride unite to the crystalline compound $(CH_3)_2C{=}CHCH_3,2ZnCl_2$. Water converts this into dimethylethyl carbinol, whilst hydrogen chloride produces the chloride of the latter. This chloride and trimethylethylene then unite to form a saturated chloride, which, on distillation, splits off hydrochloric acid and yields diamylene (Ber. **25**, R. 865).

Tetramethylethylene (Ber. **16**, 398) is produced by heating β-*iso*amylene (see p. 107) with methyl iodide and lead oxide :

$$(CH_3)_2C : CH{\cdot}CH_3 + CH_3I = (CH_3)_2C : C(CH_3)_2 + HI.$$

In the dry distillation of many complicated carbon compounds the olefines are produced together with the normal paraffins, hence their presence in illuminating gas and in tar oils (see Ethylene).

Properties and Reactions of the Olefines.—So far as physical properties are concerned, the olefines resemble the saturated hydrocarbons ; the lower members are gases, the intermediate mobile liquids, whilst the higher (from $C_{16}H_{32}$ upwards) are solids. Generally, their boiling points are a few degrees higher than those of the corresponding paraffins.

In chemical properties, on the other hand, they differ greatly from the paraffins. Being unsaturated, they can unite directly with two univalent atoms or groups, whereby the double bond becomes single.

(1) They combine with nascent hydrogen, forming paraffins with an equal number of carbon atoms.

(2) They combine with the halogen acids, especially easily with hydrogen iodide.

The halogen acids attach themselves in such a manner to the mono- and di-alkylethylenes that the halogen unites with the carbon atom combined with fewest hydrogen atoms (Ber. **39**, 2138). As such alkylethylenes can be prepared from the proper primary alcohols by the splitting-off of water, these reactions can be employed to convert primary into secondary alcohols, and also tertiary alcohols (p. 134).

The olefines are also capable of combining with the fatty acids (Ber. **25**, R. 463), but only when exposed to high temperatures (290–300°), *e.g.*:

$$\underset{\text{Amylethylene.}}{C_5H_{11}CH{=}CH_2} + CH_3{\cdot}CO_2H = \underset{\textit{sec.}\text{-Heptyl acetate.}}{C_5H_{11}CH(O{\cdot}CO{\cdot}CH_3){\cdot}CH_3}.$$

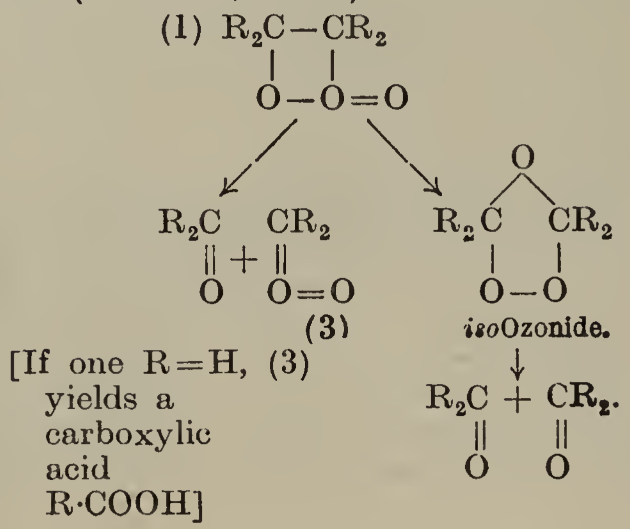
(3) Concentrated sulphuric acid absorbs them, forming ethereal salts. This is a reaction which can be used to convert olefines into alcohols, and also to separate them from paraffins, which are much more resistant to the action of sulphuric acid (C. 1899, I. 967).

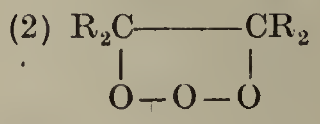
(4) They form dihalides (see Ethylene) with Cl_2, Br_2, I_2, ClI. These can be viewed as the haloid esters of the dihydric alcohols—the glycols, into which they can be converted.

(5) They yield chlorhydrins with aqueous hypochlorous acid. These are the basic esters of the glycols (see Ethylene), in which the hydroxyl is attached to the carbon atom with the fewest hydrogen atoms (C. 1901, II. 1249).

(6) They are oxidized by potassium permanganate in dilute solution to glycols. Benzoyl peroxide or benzoyl hydroperoxide in neutral solution produce ethylene oxides, which with water give glycols (Ber. **42,** 4811: C. 1911, I. 1279: II. 268).

Ozone adds at the double bond to form ozonides, which are decomposed by water into two molecules of aldehydes or ketones. Staudinger has recently put forward the view that the ozonides should be represented by the formula (1) rather than (2). This compound should then break down as illustrated to give the keto-compounds, whereas the older formulation (2) should yield a glycol derivative (Ber. **58,** 1088).





(7) With N_2O_3 and N_2O_4 the olefines unite to form pseudonitrosites $R{\cdot}CH(NO_2){\cdot}CH(NO){\cdot}R$ and dinitro compounds

$$R{\cdot}CH(NO_2){\cdot}CH(NO_2)R$$

respectively (*Wieland*, Ann. **424**, 71): nitrosyl chloride also forms addition compounds. (Ber. **12**, 169: **27**, 455: R. 467: C. 1901, II. 1201.)

(8) *Polymerization of Olefines.*—When acted on by a number of reagents, such as dilute sulphuric acid (Ber. **29**, 1550), zinc chloride (C. 1897, I. 360), boron fluoride, the higher olefines undergo polymerization, even at the ordinary temperature. Thus *iso*butylene, C_4H_8, yields di*iso*butylene, C_8H_{16}, and *iso*amylene, C_5H_{10}, yields di- and tri*iso*amylenes. Butylene and propylene similarly form polymers. These compounds, like the simple olefines from which they are derived, are unsaturated compounds. Under ordinary conditions ethylene itself does not polymerize, but when it is heated under pressure in the presence of aluminium chloride, it polymerizes, yielding not only olefines, but also paraffins and *cyclo*paraffins. The higher olefines also yield *cyclo*paraffins in the presence of aluminium chloride (Ber. **42**, 4610: **43**, 388: **44**, 2978: **46**, 1748).

(9) *Isomerization of Olefines.*—In presence of certain contact substances, some olefines undergo at high temperatures a change in constitution, either by shift of the double bond, or by the wandering of an alkyl group, *e.g.* 80 per cent. of the compound $Me_2CH{\cdot}CH:CH_2$ is changed to $Me_2C:CH{\cdot}CH_3$ over alumina at 530° (Ber. **36**, 2003: D.R.P. 263017: C. 1913, II. 729: see also Bull. Soc. chim. Belg., 1920, **29**, 192).

Below are given the boiling points of some homologues of ethylene.

		B.P.
Propylene	$CH_3{\cdot}CH{=}CH_2$	− 48°
α-Butylene (Ethylethylene) . .	$CH_3{\cdot}CH_2{\cdot}CH{=}CH_2$	− 5°
β-Butylene (Dimethylethylene) .	$CH_3{\cdot}CH{=}CH{\cdot}CH_3$	+ 1° (*cis*)
		+ 2·5° (*trans*)
*iso*Butylene (*as*-Dimethylethylene) .	$(CH_3)_2C{=}CH_2$	− 6°
α-Amylene (Propylethylene) . .	$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH{=}CH_2$	+ 39°
β-Amylene (*sym*-Methylethylethylene)	$CH_3{\cdot}CH_2{\cdot}CH{=}CH{\cdot}CH_3$	+ 36°
γ-Amylene (*as*-Methylethylethylene)	$CH_3{\cdot}CH_2{\cdot}CMe{=}CH_2$	+ 31°
α-*iso*Amylene (*iso*Propylethylene) .	$(CH_3)_2CH{\cdot}CH{=}CH_2$	+ 21°
β-*iso*Amylene (Trimethylethylene) .	$(CH_3)_2C{=}CHCH_3$	+ 36°
Tetramethylethylene . . .	$(CH_3)_2C{=}C(CH_3)_2$	+ 73°
tert-Butylethylene	$CMe_3{\cdot}CH{=}CH_2$	+ 41°

Many higher members of this series are known. β-*iso*Amylene, which is the principal constituent of the mixture of olefines obtained by dehydration of the amyl alcohol of fermentation, is of importance because of its use in the preparation of so-called *amylene hydrate* or tertiary amyl alcohol.

Tetramethylethylene is formed from pinacolyl alcohol,

$$CMe_3CHOH{\cdot}CH_3$$

by loss of water. In this reaction a migration of a methyl group takes place, in the opposite direction to that involved in the pinacone-pinacolin change (*q.v.*). For a discussion of the mechanism of this change, see C. 1908, I. 113.

HYDROCARBONS, C_nH_{2-n2}

Two groups of hydrocarbons having this empirical formula exist :
The *acetylenes* or alkines with triple linking, and
The *diolefines* with two double linkages.

The difference in structure is clearly shown in their different chemical behaviour. The acetylenes (with group $\equiv CH$) alone have the power of entering into combinations in which the hydrogen of the group $\equiv CH$ is replaced by metals. The names adopted for the acetylenes by the Geneva Congress are formed by substituting the ending "ine" for the ending *yl* of alcohol radicals with like carbon content, hence the designation alkines.

2. ACETYLENES OR ALKINES, C_nH_{2n-2}

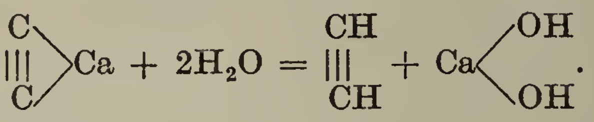
The position of acetylene, the first member of this series, among the aliphatic hydrocarbons is very prominent, on account of its technical importance, and its direct formation from carbon and hydrogen.

Acetylene [*Ethine*] $CH\equiv CH$ was first observed by *Edmund Davy*. *Berthelot* introduced the name acetylene and studied the hydrocarbon carefully.

(1) Berthelot effected the synthesis of acetylene by passing the electric arc between carbon points in an atmosphere of hydrogen (p. 83) :

$$2C + H_2 = CH\equiv CH.$$

(2) It results from the decomposition of the carbides of the alkaline earths by water :



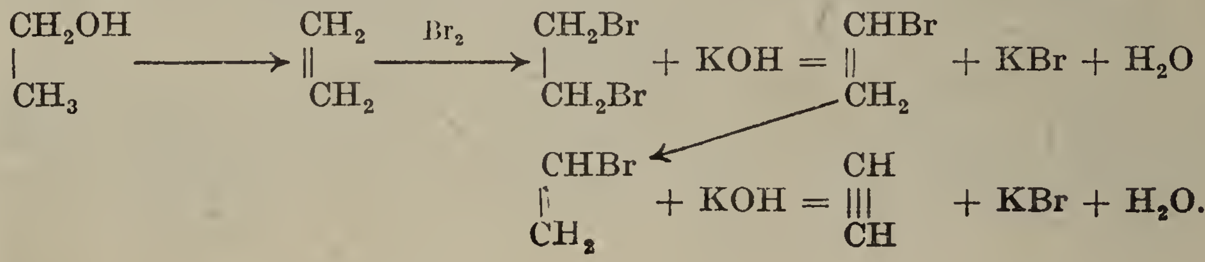
$$\begin{matrix}C\\ |||\\ C\end{matrix}\!>\!Ca + 2H_2O = \begin{matrix}CH\\ |||\\ CH\end{matrix} + Ca\!<\!\begin{matrix}OH\\ OH\end{matrix}.$$

The addition of formaldehyde solution retards the evolution of acetylene from calcium carbide (C. 1900, II. 1150). The gas is always contaminated by phosphine, which can be removed by the action of bromine water, or better by means of a feebly acid solution of copper sulphate and of chromic acid in sulphuric acid (C. 1900, I. 789 : Ber. **32**, 1879). On a large scale bleaching powder or bleaching powder and lead chromate (to avoid the evolution of free chlorine) are recommended as purifiers (C. 1900, I. 236 : II. 229).

(3) It may be prepared from methane by converting it into chloroform, from which chlorine is removed by means of red-hot copper or heated metallic sodium (Fittig). Bromoform, $CHBr_3$, and iodoform, CHI_3, are very readily changed by silver or zinc dust into acetylene :

$$2CH_4 \longrightarrow 2CHCl_3 \longrightarrow \begin{matrix}CH\\ |||\\ CH\end{matrix}.$$

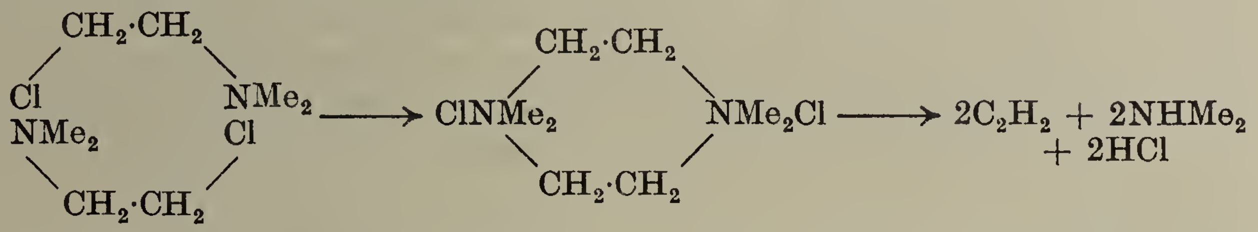
(4) Formerly acetylene was always made from ethylene bromide by the action of alcoholic potassium hydroxide (Ann. **191**, 268). At first the ethylene bromide loses a molecule of hydrogen bromide and becomes monobromoethylene or vinyl bromide, which in turn loses a molecule of hydrogen bromide with the production of acetylene :



$$\begin{matrix}CH_2OH\\ |\\ CH_3\end{matrix} \longrightarrow \begin{matrix}CH_2\\ \|\\ CH_2\end{matrix} \xrightarrow{Br_2} \begin{matrix}CH_2Br\\ |\\ CH_2Br\end{matrix} + KOH = \begin{matrix}CHBr\\ \|\\ CH_2\end{matrix} + KBr + H_2O$$

$$\begin{matrix}CHBr\\ \|\\ CH_2\end{matrix} + KOH = \begin{matrix}CH\\ |||\\ CH\end{matrix} + KBr + H_2O.$$

(5) Acetylene is also obtained when quaternary piperazonium salts, which are obtained by the polymerization of dimethylchloroethylamine are boiled with alkali (*Knorr*, Ber. **37,** 3507).



(6) Acetylene is also produced by electrolysis of the alkali salts of the stereoisomeric maleic and fumaric acids (*Kekulé*, Ann. **131,** 85).

$$\begin{array}{l}CH\vdots CO_2\vdots K\\ \|\\ CH\vdots CO_2\vdots K\end{array} + \begin{array}{l}HO\vdots H\\ \\ HO\vdots H\end{array} \longrightarrow \begin{array}{c}CH\\ |||\\ CH\end{array} + 2CO_2 + 2KOH + H_2.$$

(7) Acetylene is evolved by the action of sodium hydroxide solution on propargyl aldehyde :

$$CH{\equiv}C{\cdot}CHO + HONa \longrightarrow CH{\equiv}CH + H{\cdot}COONa.$$

(8) Potassium acetylene-monocarboxylate and silver acetylene-dicarboxylate are decomposed on warming with water with the formation of acetylene and silver acetylide respectively.

$$AgO_2C{\cdot}C{\equiv}C{\cdot}CO_2Ag \longrightarrow AgC{\equiv}CAg + 2CO_2.$$

(9) Acetylene is also formed when the vapours of many carbon compounds such as alcohol, ether, methane, ethylene, etc., are passed through tubes heated to redness. Hence it is present in small amount in illuminating gas, to which it imparts a peculiar odour.

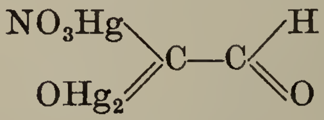
Properties.—Pure acetylene is a gas of agreeable ethereal odour. It liquefies at + 1° under a pressure of 48 atm. The liquid solidifies when rapidly vaporized, and then sublimes at − 82°. Its critical temperature is + 35·5° and critical pressure 61·5 atm. It is strongly endothermic, and under certain conditions decomposes with great heat and sudden increase in volume. It should not be compressed in cylinders on account of the danger of explosion, but may be dissolved safely in acetone, in which it is readily soluble. It is slightly soluble in water, more readily in alcohol, ether, acetal and ethyl acetate. It burns with a smoky flame, and forms an exceedingly explosive mixture with air over a range of composition 2·5 to 65 per cent. and with oxygen over a range 2 to 98 per cent.

It is largely used for cutting and welding metals, and more recently has been used as a general anæsthetic under the name *narcylene.*

Reactions.—Nascent hydrogen converts acetylene into C_2H_4 and C_2H_6. Ordinary hydrogen (2 vols.) and acetylene (1 vol.), passed over platinum black, form C_2H_6 (Ber. **7,** 352). Finely divided Ni, Co, Fe, and Cu behave similarly (C. 1899, I. 1270 : 1900, II. 528), producing at the same time high molecular cork-like condensation products (Ber. **32,** 2381). Acetylene combines with HCl and HI, forming CH_3CHCl_2 and CH_3CHI_2.

Acetylene reacts with chlorine gas in the sunlight with a slight explosion. It forms a crystalline compound with $SbCl_5$, which is changed by heat into dichlorethylene, CHCl : CHCl, and $SbCl_3$. With bromine it forms $C_2H_2Br_2$ and $C_2H_2Br_4$ (Ann. **221,** 138).

In contact with $HgBr_2$ and other mercury salts acetylene unites with water to yield aldehyde, which is also produced when acetylene alone is heated with water to 325°, or when it is passed into dilute sulphuric acid in presence of HgO (C. 1898, II. 1007). Fuming sulphuric acid absorbs acetylene, forming acetaldehyde di-sulphonic acid and methionic acid (*q.v.*). With HClO and HBrO acetylene forms dichlor- and dibromacetaldehyde (C. 1900, II. 29). Acetylene unites with an aqueous solution of mercuric nitrate to form a substance—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which can also be obtained from acetaldehyde ; similarly, trichloromercuriacetaldehyde $(ClHg)_3C{\cdot}CHO$ is produced with mercuric chloride solution (Ber. **37**, 4417). In the case of mercuric nitrite or chlorate, however, the similar compounds which are formed, are explosive (Ber. **38**, 1999). In diffused daylight, contact with potassium hydroxide solution and air, acetylene changes into acetic acid. Oxidation with nitric acid leads to the formation of nitroform $CH(NO_2)_3$, and other bodies (J.C.S. **117**, 283). Acetylene unites with diazomethane, forming pyrazole. With ozone, if sufficiently dilute, glyoxal is formed (Chem. Ztg. **44**, 157). For other reactions, see also diagram, p. 113.

Acetylene polymerizes at a red heat, three molecules uniting to form one molecule of benzene, C_6H_6. This is one of the most striking transitions from the aliphatic to the aromatic series and, at the same time, constitutes a synthesis of the parent hydrocarbon of aromatic substances (Berthelot). By the use of activated charcoal, the yield of condensation product can be raised to 70 per cent. (Zelinsky, Ber. **57**, 264).

This conversion will take place at the ordinary temperature if acetylene be passed over pyrophoric iron, nickel, cobalt, or platinum sponge (Ber. **29**, R. 540 ; see also above).

Metallic Derivatives of Acetylene.—The two hydrogen atoms of acetylene can be replaced by metals. The alkali and alkali earth acetylides are stable even when heated, but are decomposed by water with the liberation of acetylene. Copper and silver acetylides when dry are exceedingly explosive, but are stable in the presence of water. Acids evolve pure acetylene from them.

Calcium Acetylide or **Calcium Carbide,** C_2Ca, is formed when calcium oxide is reduced by carbon at a red heat (Wöhler, 1862), and when a mixture of calcium oxide and sugar carbon is heated in electric furnaces to 3500° (Moissan, Ber. **27**, R. 238 : C. 1899, II. 1093). It is a homogeneous mass, colourless in its purest form but usually obtained of a grey tint, and shows a crystalline fracture. If fragments of calcium carbide are dropped into a tall glass cylinder filled with saturated chlorine water, the liberated acetylene will combine with the chlorine with the production of flame. Gas-bubbles, giving out light, rise in the liquid and when they reach the surface burn there with a smoky flame. German production in 1923, 570,000 tons.

Sodium Acetylides, $CH{\equiv}CNa$ and $CNa{\equiv}CNa$, are produced when sodium is heated in acetylene gas (C. 1897, I. 966 : 1899, I. 174 : 1904, II. 1204). Sodium acetylide is also formed when acetylene is passed into a solution of sodium in liquid ammonia, ethylene being simultaneously formed (Compt. rend. **127**, 911 : **157**, 137). *Lithium Carbide*, C_2Li_2, is obtained from lithium carbonate and carbon (Ber. **29**, R. 210). *Cæsium Carbides*, C_2HCs and C_2Cs_2, and *Rubidium Carbides*, C_2HRb and C_2Rb_2, are produced when acetylene is led into solutions of cæsium-ammonium and rubidium-ammonium in ammonia (C. 1903, II. 105).

Silver Acetylide, C_2Ag_2, a white precipitate, and **Copper Acetylide**, C_2Cu_2 (Ber. **25**, 1097 : **26**, R. 608 : **27**, R. 466), a red precipitate, are formed when acetylene is conducted into ammoniacal silver or cuprous chloride solutions. The dry salts explode violently when they are heated ; the silver salt even does this when gently rubbed with a glass rod. In a solution of silver nitrate acetylene precipitates the compound $HC{\equiv}CAg{\cdot}AgNO_3$ (Ber. **28**, 2108). *Gold Acetylide*, C_2Au_2, a yellow precipitate, is obtained from acetylene and a solution of ammoniacal gold-sodium thiosulphate (C. 1900, I. 755). Pure acetylene is set free by acids from these metallic compounds. The copper salt serves for the detection of acetylene in a mixture of gases. *Mercury Acetylide*, C_2Hg, is thrown out as a white precipitate from alkaline solutions of mercuric oxide. It explodes violently when heated rapidly.

Magnesium derivative.—By passing acetylene into an ethereal solution of magnesium ethyl bromide, acetylene dimagnesium dibromide, $BrMgC : CMgBr$, is produced, with evolution of ethane. This is decomposed by water with formation of acetylene, and can be used like other organomagnesium compounds (see p. 219) for the synthesis of substances with an acetylenic linkage (Bull. Soc. Chim. [3], **28**, 922 : **30**, 208 : Gazzetta, **38**, I. 625).

Acetylene Homologues

The acetylene homologues are isomeric with the corresponding diolefines. Thus allylene (methylacetylene) $CH ⋮ C{\cdot}CH_3$ is isomeric with allene, $CH_2 : C : CH_2$, and crotonylene (dimethylacetylene), $CH_3{\cdot}C ⋮ C{\cdot}CH_3$, with butadiene, $CH_2 : CH{\cdot}CH : CH_2$.

The homologues, like acetylene itself, are mostly prepared from the monohalogen substitution products, and the dihalogen addition products of the olefines by removal of halogen acid, by means of alcoholic potassium hydroxide, *e.g.* from β-chloropropylene, $CH_2 : CCl{\cdot}CH_3$, allylene is obtained. A large number of olefines have been prepared by this method (Ber. **33**, 3586). The acetylenes are also prepared by the removal of two molecules of halogen acid from the aldehyde or ketone chlorides, $R{\cdot}CCl_2{\cdot}R$, *e.g.* heptylidene chloride, $CH_3[CH_2]_5CHCl_2$, yields heptine, $CH_3[CH_2]_4C ⋮ CH$ (J.A.C.S. **50**, 1744).

A more recent method for the preparation of homologous acetylenes is the action of calcium carbide on methyl alcohol vapour at temperatures greater than 100°.

$$CaC_2 + 2CH_3OH = Ca(OH)_2 + C_4H_6.$$

(Z. angew. Chem. **34**, 403 : J. pr. Chem. **37**, 382.)

When strongly heated with alkalis the acetylene formed frequently undergoes an isomeric change ; thus, ethylacetylene, $C_2H_5{\cdot}C{\equiv}CH$, yields dimethylacetylene, $CH_3{\cdot}C{\equiv}C{\cdot}CH_3$, and propylacetylene, $C_3H_7{\cdot}C{\equiv}CH$, furnishes ethylmethylacetylene, $C_2H_5{\cdot}C{\equiv}C{\cdot}CH_3$, etc. (Ber. **20**, R. 781). More symmetrical compounds are formed from less symmetrical.

The reverse transposition sometimes occurs on heating with metallic sodium ; ethylmethyl acetylene passes into propyl acetylene, and dimethyl allene, $(CH_3)_2C{=}C{=}CH_2$, yields *iso*propylacetylene, etc.

Acetylenes are also formed in the electrolysis of unsaturated dibasic acids : thus, allylene is formed in the electrolysis of the alkali salts of mesaconic and citraconic acids.

A number of acetylenes have also been prepared by the action of alkyl iodides on sodium acetylide dissolved in liquid ammonia (*Picon*, Compt. rend. **158**, 1184, 1346 : **168**, 894 : **169**, 32).

Acetylene and its homologues combine with hydrogen, forming first olefines, which on further reduction yield paraffins. They combine also with halogens and halogen acids, yielding substitution products of the olefines : these are capable of further addition of halogen or halogen acid, yielding di- tri- and tetra-halogen substitution products of the paraffins.

Hypochlorous and hypobromous acids yield dichloro- and dibromo-ketones, *e.g.* allylene with hypobromous acid gives *as*-dibromoacetone, $CH_3COCHBr_2$ (C. 1900, II. 29). Vinylsulphuric acid, $CH_2 : CH\cdot SO_4H$, is formed almost quantitatively when cold anhydrous sulphuric acid is saturated with acetylene below 0° in presence of a catalyst such as $HgSO_4$ (*Brit. Pat.* 156121). Some of the higher acetylenes are polymerized into symmetrical benzene derivatives by concentrated sulphuric acid. Thus allylene yields mesitylene (trimethylbenzene)

$$3CH \vdots C\cdot CH_3 \longrightarrow C_6H_3(CH_3)_3$$

and crotonylene similarly yields hexamethylbenzene.

The monoalkyl acetylenes, like the parent substance, readily form solid crystalline silver and copper derivatives by their action on ammoniacal solutions of silver and cuprous salts. They are regenerated from these by warm hydrochloric acid, and the formation of these compounds affords a convenient method for obtaining the pure acetylenes from a mixture of gases. The monoalkyl acetylenes also react with magnesium ethyl bromide similarly to acetylene, with evolution of ethane and formation of $R\cdot C \vdots C\cdot MgBr$.

In the presence of various salts of mercury, the acetylenes unite with water, yielding ketonic compounds. Thus, acetylene yields acetaldehyde, CH_3CHO, allylene yields acetone, $CH_3\cdot CO\cdot CH_3$. Very often, moderately diluted sulphuric acid brings about the same reaction. Methyl-*n*-propylacetylene yields two isomeric ketones when treated with about 80 per cent. sulphuric acid (Ber. **39**, 2147). When heated with water at 325° the alkylacetylenes yield ketones (Ber. **27**, R. 750 : **28**, R. 173).

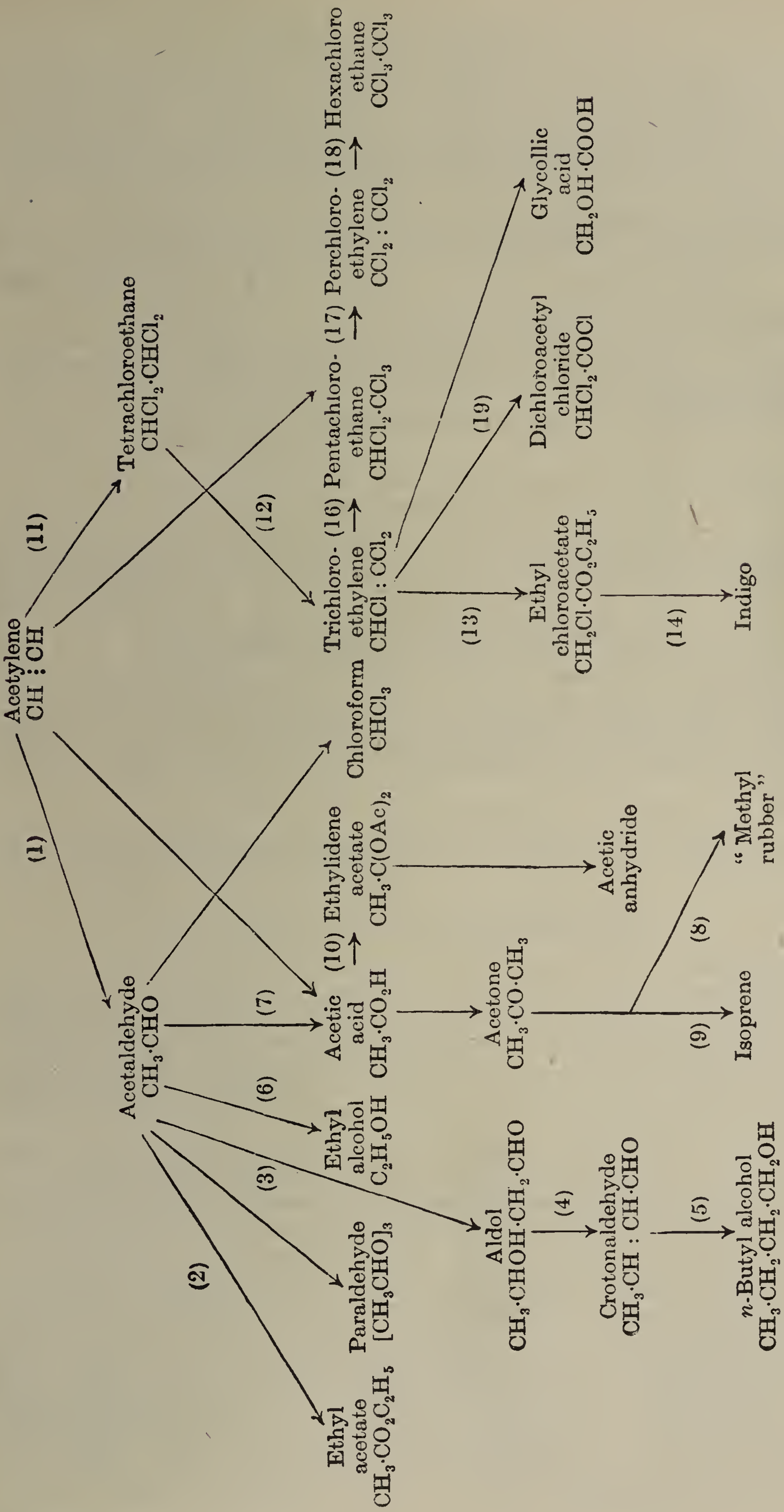
The sodium acetylides react with acid chlorides, trioxymethylene, and carbon dioxide to form respectively acetylenic ketones, $R\cdot C \vdots C\cdot CO\cdot R'$, acetylenic alcohols, $R\cdot C \vdots C\cdot CH_2OH$, and acetylenecarboxylic acids, $R\cdot C \vdots C\cdot COOH$. Higher alkylacetylenes, see Ber. **25**, 2245 : **33**, 3586.

The boiling points of some of the acetylenes are as follows :

		B.P.
Allylene, Methylacetylene [Propine] . . .	$CH_3C\equiv CH$	Gas
Crotonylene, Dimethylacetylene [Δ^β-Butine] . .	$CH_3C\equiv CCH_3$	27°
Ethylacetylene [Δ^α-Butine]	$C_2H_5C\equiv CH$	18°
Methylethylacetylene [Δ^β-Pentine]	$C_2H_5C\equiv CCH_3$	55°
n-Propylacetylene [Δ^α-Pentine] . . .	n-$C_3H_7C\equiv CH$	48°
*iso*Propylacetylene [γ-Methyl-Δ^α-butine] . .	$(CH_3)_2CH\cdot C\equiv CH$	28°
Methyl-*n*-propylacetylene [Δ^β-Hexine] . .	n-$C_3H_7C\equiv C\cdot CH_3$	84°

REFERENCES TO TABLE ON PAGE 113.

(1) Dilute sulphuric acid in presence of mercuric sulphate (Ber. **14**, 1540 and various patents). (2) Aluminium alcoholate (C. 1918, II. 693 : 1924, I. 1504). (3) Alkalis (C. 1914, I. 716). (4) Distillation under atmospheric pressure. (5) Catalytic hydrogenation with nickel (C. 1912, I. 20). (6) as (5). (7) Catalytic oxidation in presence of metallic oxides (C. 1914, II. 324 : 1920, II. 187). (8) Polymerization by heat. (9) Merling's isoprene synthesis : see Z. angew. Chem. **34**, 403. (10) Action of acetylene on acetic acid in presence of mercuric salts (C. 1914, I. 1316). (11) Chlorine and acetylene in presence of $SbCl_5$ (D.R.P. 157, 657). (12) Heating with alkali (C. 1906, II. 571). (13) Action of alkali to form dichlorovinyl ether (p. 158) hydrolysis with water (C. 1909, I. 1784 : 1920, III. 408). (14) See Vol. III. (15) Heating with alkali. (16) Chlorination of trichloroethylene, or directly from acetylene. (17) Heating with alkali. (18) Chlorination of perchloroethylene. (19) Chem. Ztg. **35**, 1052.



PRODUCTS OBTAINABLE FROM ACETYLENE

3. DIOLEFINES. C_nH_{2n-2}

The diolefines are distinguished from the isomeric acetylenes by their inability to form copper and silver derivatives. Some of them, however, form precipitates with aqueous mercuric chloride solutions, which are identical with the compounds formed from the corresponding acetylenes.

According to the relative position of the double bonds in the molecule, the diolefines can be divided into the following classes.

I. Hydrocarbons with two double bonds joined to the same carbon atom—the *allene* hydrocarbons.

II. Hydrocarbons with double bonds attached to adjacent carbon atoms—*i.e.* "conjugated" double bonds—the *butadiene* hydrocarbons.

III. Hydrocarbons with separated double bonds.

I. Allene Hydrocarbons

The allene hydrocarbons can be prepared from the corresponding allyl alcohol by the following general method. The alcohol (I) is treated with phosphorus tribromide to give the bromide (II) (with a simultaneous shift in the position of the double bond). This compound adds on bromine to form the tribromo- compound (III), from which hydrobromic acid is removed by fusion with potassium hydroxide, the remaining bromine atoms being removed from the product (IV) by zinc dust and boiling alcohol (*Bouis*, Ann. Chim. 1928 [x], 9, 402).

$$\underset{(I)}{R{\cdot}CH(OH){\cdot}CH : CH_2} \xrightarrow{PBr_3} \underset{(II)}{R{\cdot}CH : CH{\cdot}CH_2Br} \xrightarrow{Br_2} \underset{(III)}{R{\cdot}CHBr{\cdot}CHBr{\cdot}CH_2Br}$$

$$\xrightarrow{KOH} \underset{(IV)}{R{\cdot}CHBr{\cdot}CBr : CH_2} \longrightarrow \underset{(V)}{R{\cdot}CH : C : CH_2}$$

Allene (*Propadiene*), $CH_2 : C : CH_2$, boils at − 32° and melts at − 146°. It is formed by removal of bromine from dibromopropylene, $CH_2 : CBr{\cdot}CH_2Br$, by means of zinc dust, by electrolysis of potassium itaconate, or by heating bromomethacrylic acid. In contradistinction to allylene, $CH_3C : CH$, it is not absorbed by ammoniacal silver solution, but with mercuric chloride it yields a white mercury salt, which, when decomposed with hydrochloric acid, gives acetone (Ann. **342**, 185).

The allene hydrocarbons polymerize very readily, forming products whose constitution is not at present clear (Lebedew, C. 1914, I. 1402, 1813).

The boiling point of some homologous allenes is given below. Others are referred to in the paper of Bouis (see above).

		B.P.	
Methylallene ($\Delta^{\alpha\beta}$-butadiene)	$CH_3CH : C : CH_2$	18°	Ber. **22**, R. 202
Ethylallene ($\Delta^{\alpha\beta}$-pentadiene)	$C_2H_5CH : C : CH_2$	44°	
sym-Dimethylallene	$CH_3CH : C : CH{\cdot}CH_3$	51°	C. 1914, I. 1409
as-Dimethylallene	$(CH_2)_2C : C : CH_2$	41°	J. pr. Chem. [2], **53**, 149
Trimethylallene	$(CH_3)_2C : C : CHCH_3$	72°	C. 1914, I. 1409
Tetramethylallene	$(CH_3)_2C : C : C(CH_3)_2$	86°	C. 1914, I. 1813

II. Hydrocarbons with Conjugated Double Bonds

Among these hydrocarbons, *isoprene* $CH_2 : CMe{\cdot}CH : CH_2$ is of particular importance, because of its relationship to the terpenes on the one hand, and the fact that it can be converted into a product very closely related to natural rubber on the other (*cf. Harries,* Untersuchungen über die natürlichen und künstlichen Kautschukarten, Berlin, 1919).

General Methods of Formation.

(1) The butadienes are obtained by splitting off two molecules of halogen acid from the appropriate dihalogen paraffins by heating with alcoholic potash, pyridine or quinoline, or by passing their vapours over soda-lime or other contact substance (D.R.P. 255519, 264008: C. 1913, I. 476: II. 1178).

(2) They are formed from the alkylenediamines, by heating the phosphates, or by "exhaustive methylation" and distillation of the quaternary ammonium hydroxides. The formation of butadiene and isoprene from pyrrolidine and 3-methylpyrrolidine are essentially similar methods.

$$NH_2{\cdot}[CH_2]_4{\cdot}NH_2 \longrightarrow HONMe_3{\cdot}[CH_2]_4{\cdot}NMe_3OH$$
$$\longrightarrow CH_2 : CH{\cdot}CH : CH_2 + 2H_2O + 2NMe_3$$

(3) From the paraffin glycols or the unsaturated alcohols by removal of water by means of zinc chloride, potassium hydrogen sulphate or oxalic acid, or by distilling them over heated alumina (J.A.C.S. 1914, **36,** 980).

$$(CH_3)_2C(OH){\cdot}C(OH)(CH_3)_2 \longrightarrow CH_2{=}C(CH_3){\cdot}C(CH_3) : CH_2 + 2H_2O$$

(4) By passing a mixture of an alcohol and an aldehyde over heated alumina (C. 1916, I. 831).

$$CH_3{\cdot}CHO + (CH_3)_2{\cdot}CHOH \longrightarrow CH_3{\cdot}CHOH{\cdot}CH_2{\cdot}CHOH{\cdot}CH_3$$
$$\longrightarrow CH_2 : CH{\cdot}CH : CH{\cdot}CH_3 \text{ (Piperylene)}$$

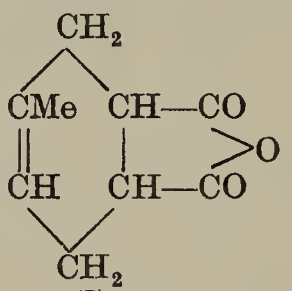
(5) By exhaustive methylation of the hydroxy and halogen alkylamines, and subsequent decomposition of the quaternary ammonium hydroxide.

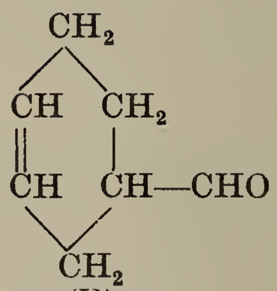
(6) By the thermal decomposition of some tetrahydrobenzene derivatives.

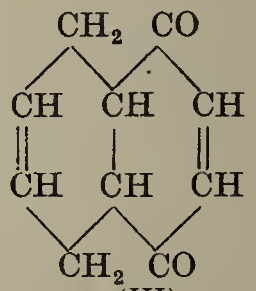
(7) By heating together equimolecular quantities of ethylenic and acetylenic hydrocarbons (E.P. 156116: C. 1921, II. 655).

Properties.—With the exception of the first member, which is a gas, the butadienes are colourless, mobile liquids. They have a high optical dispersion (see p. 67). They combine with two or four equivalents of hydrogen, bromine, etc., the addition taking place chiefly in the $\alpha\delta$-position, butadiene for example giving $CH_2Br{\cdot}CH : CH{\cdot}CH_2Br$ (Ann. **308,** 333). Their most important property is their great tendency to polymerize (C. 1914, I. 1402); according to the conditions substances similar to rubber or hydroaromatic compounds are produced. A compound apparently identical with natural rubber and a monoterpene, dipentene, which occurs widely in various essential oils can be obtained from isoprene (Harries, *loc. cit.*).

Diels and Alder and their collaborators have recently shown that compounds containing a conjugated system of double bonds unite quantitatively with compounds containing the $CH : CH{\cdot}CO$ group with the formation of cyclic compounds. The addition takes place wholly in the $\alpha\delta$-position. Examples of the type of compound formed are those from isoprene and maleic anhydride (I), from butadiene and acraldehyde (II), and from butadiene and *p*-benzoquinone (III) (Ann. 1928, **460,** 98: 1929, **470,** 62: Ber. 1929, **62,** 554, 2081: *cf.* Annual Reports, 1930, 88).


(I)


(II)


(III)

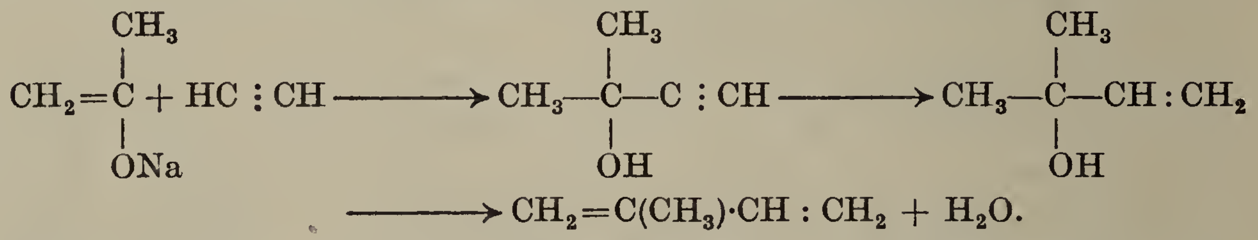
$\Delta^{\alpha\gamma}$-**Butadiene** (*Erythrene, Divinyl, Pyrrolylene*), $CH_2 : CH{\cdot}CH : CH_2$, b.p. − 5°. It is obtained by exhaustive methylation of the cyclic base pyrrolidine (Vol. II) (Ber. **14,** 569: Ann. **308,** 333). It is also obtained by passing a mixture of ethylene and acetylene through red-hot tubes and occurs in compressed illuminating gas. It is also formed by passing ethyl ether or monochloroethyl ether over heated alumina (C. 1914, I. 2155). New methods for the preparation of butadiene are given by Ostromysslenski (C. 1916, I. 780).

Butadiene is the starting material for the synthesis of erythritol and can be re-formed from the latter by heating it with formic acid.

The *tetrabromide* occurs in two stereoisomeric forms, m.pp. 39° and 119°. For further details about the polymerization of butadiene, see C. 1912, I. 1440.

Piperylene ($\Delta^{\alpha\gamma}$-*Pentadiene*), $CH_3{\cdot}CH : CH{\cdot}CH : CH_2$, b.p. 42° (Ann. **395,** 243), is formed from piperidine in the same way as butadiene from pyrrolidine (Ber. **14,** 665, 710: Ann. **319,** 226). This reaction might be expected to yield the still unknown hydrocarbon $\Delta^{\alpha\delta}$-pentadiene, $CH_2 : CH{\cdot}CH_2{\cdot}CH : CH_2$.

Isoprene (β-*Methylbutadiene*), $CH_2 : C(CH_3){\cdot}CH : CH_2$, b.p. 33·75° $D_4^{16\cdot5}$ 0·6867 (Ber. **47,** 1999), is formed not only by the general reactions described above, but occurs among the products of distillation of rubber, and is formed by the thermal decomposition of pinene and dipentene (Ber. **44,** 2212: Ann. **383,** 228: C. 1914, II, 325) and from the degradation of 3-methylpyrrolidine (C. 1898, I. 247: 1897, II. 739). Isoprene is also formed by isomeric change of the hydrocarbons *as*-dimethylallene $C(CH_3)_2 : C : CH_2$ and *iso*propylacetylene by passing their vapours over heated alumina (D.R.P. 251216, 268101, 268102: C. 1912, II. 1244: 1914, I. 308, 754). It is manufactured on the large scale from *p*-cresol (Elberfelder Farbwerke: see Vol. II) or from acetylene and acetone according to the following reactions (Merling) (Z. angew. Chem. **34,** 403):



$$CH_2{=}\underset{ONa}{\overset{CH_3}{\overset{|}{\underset{|}{C}}}} + HC : CH \longrightarrow CH_3{-}\underset{OH}{\overset{CH_3}{\overset{|}{\underset{|}{C}}}}{-}C : CH \longrightarrow CH_3{-}\underset{OH}{\overset{CH_3}{\overset{|}{\underset{|}{C}}}}{-}CH : CH_2$$

$$\longrightarrow CH_2{=}C(CH_3){\cdot}CH : CH_2 + H_2O.$$

Isoprene changes into rubber or rubber-like compounds when heated under pressure, treated with sodium and carbon dioxide, or treated with peroxides or ozonides (*cf.* Z. angew. Chem. **27,** 153). A part of the isoprene is polymerized under these conditions to dipentene. Isoprene combines with two molecules of hydrogen bromide to give $\alpha\gamma$-dibromo-γ-methylbutane, $(CH_3)_2CBr{\cdot}CH_2{\cdot}CH_2Br$

(C. 1897, I. 457) and with bromine to yield a di- and a tetrabromide (C. 1900, I. 859). Thermal decomposition of isoprene (see Ber. **46**, 2466).

$\beta\gamma$-Dimethylbutadiene, $CH_2 : CMe{\cdot}CMe : CH_2$, b.p. 71°, is most readily obtained by the removal of water from pinacone (Ann. **383**, 182).

Other hydrocarbons with conjugated double bonds. A number of these have been obtained by the action of alkyl magnesium halides on $\alpha\beta$-unsaturated aldehydes and ketones, followed by removal of water from the unsaturated alcohol obtained (Ber. **37**, 3578 : **41**, 2703 : **43**, 1574, 2330 : **45**, 625).

III. Other Hydrocarbons with two Double Bonds

Diallyl ($\Delta^{\alpha\epsilon}$-*Hexadiene*), $CH_2 : CH{\cdot}CH_2{\cdot}CH_2CH : CH_2$, b.p. 59°, is obtained from allyl iodide or bromide by means of sodium or magnesium (Ann. Chim. Phys. [8] **27**, 137). Its diozonide can be broken down to give succindialdehyde (Ann. **343**, 360).

$\beta\zeta$-Dimethyl-$\Delta^{\alpha\epsilon}$-heptadiene, $Me_2C : CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe : CH_2$, b.p. 141°, is obtained from methylheptenone by the action of magnesium methyl iodide and subsequent removal of water : its diozonide yields levulaldehyde (Ann. **343**, 362).

$\beta\epsilon$-Dimethyl-$\Delta^{\alpha\epsilon}$-hexadiene, $CH_2 : CMe{\cdot}CH_2{\cdot}CH_2{\cdot}CMe : CH_2$, b.p. 137°, is obtained, together with an isomeric hydrocarbon by removal of hydrogen bromide from $\beta\epsilon$-dibromo-$\beta\epsilon$-dimethylhexane : its diozonide gives formaldehyde and acetylacetone (Ann. **343**, 365).

4. HYDROCARBONS, C_nH_{2n-4}

I. Olefineacetylenes

Vinylacetylene, $CH \vdots C{\cdot}CH : CH_2$, b.p. 2·5°, is obtained by the distillation *in vacuo* of the quaternary ammonium hydroxide from tetramethyldiaminobutene. The latter is obtained from $\alpha\delta$-dibromo-Δ^{β}-butene and dimethylamine.

$$HONMe_3{\cdot}CH_2CH : CH{\cdot}CH_2{\cdot}NMe_3OH \longrightarrow CH \vdots C{\cdot}CH : CH_2 + 2H_2O + 2NMe_3$$

It yields *copper* and *silver* salts (Ber. **46**, 535).

II. Triolefines

$\Delta^{\alpha\gamma\epsilon}$-Hexatriene, $CH_2 : CH{\cdot}CH : CH{\cdot}CH : CH_2$, b.p. 77·5–79°, is obtained by heating divinylethylene glycol diformate. *Cis* and *trans* forms have been obtained by the reduction of $\gamma\delta$-dibromo- and $\alpha\zeta$-dibromohexadienes (J.C.S. **90**, 722 : **1927**, 2937).

$\Delta^{\alpha\gamma\epsilon}$-Heptatriene, m.p. – 14·5°, is obtained by removing water from the alcohol resulting from the interaction of crotonaldehyde, allyl iodide and zinc (Chem. Weekblad, 1913, **10**, 187).

$\beta\zeta$-Dimethyl-δ-methylene-$\Delta^{\beta\epsilon}$-heptadiene, $Me_2C{:}CH{\cdot}C({:}CH_2){\cdot}CH{:}CMe_2$, b.p. 55–57°/14 mm., is obtained from phorone and methylmagnesium iodide (Ber. **37**, 3578).

5. HYDROCARBONS, C_nH_{2n-6}

I. Diacetylenes

Diacetylene, $CH \vdots C{\cdot}C \vdots CH$, is obtained from diacetylenedicarboxylic acid, or more conveniently by oxidizing copper acetyleide with cupric chloride. It is a gas, m.p. – 36°, b.p. 9·5°/749 mm. which, like acetylene, forms a silver derivative.

Dipropargyl, $CH \vdots C{\cdot}CH_2{\cdot}CH_2{\cdot}C \vdots CH$, m.p. – 8°, b.p. 85°, is formed on warming solid crystalline diallyl tetrabromide, $C_6H_{10}Br_4$, with aqueous potassium hydroxide. It is a very mobile liquid, of penetrating odour. It forms copper and silver derivatives. If dipropargyl be allowed to stand, it becomes resinous.

Dimethyldi-acetylene, $CH_3{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH_3$, m.p. 64°, b.p. 130°, has been obtained from the copper derivative of allylene (Ber. **20**, R. 564).

II. Diolefineacetylenes

A number of diolefineacetylenes have been obtained by the removal of water from acetylenic glycols (D.R.P. 241424, C. 1912, I. 173).

6. STILL MORE UNSATURATED HYDROCARBONS

Two highly unsaturated hydrocarbons, squalene and lycopene, are of considerable biological importance.

Squalene, $C_{30}H_{50}$. This is obtained from the unsaponifiable fraction of fish-liver oils, and has the probable formula :

$$(CMe_2 : [CH{\cdot}CH_2CH_2CMe]_2 : CH{\cdot}CH_2)_2$$

(J.C.S. **1929**, 873 : Helv. Chim. Acta. 1930, **13**, 1084).

Lycopene, $C_{40}H_{56}$, occurs in tomatoes. It has most probably the constitution :

$$(CMe_2 : CH{\cdot}[CH_2]_2{\cdot}CMe : CH{\cdot}[CH : CH{\cdot}CMe : CH]_2{\cdot}CH :)_2$$

(Helv. Chim. Acta. 1930, **13**, 1084). An isomer of lycopene, but one which contains two carbon rings, is *carotene*, found in carrots, and in the leaves of many other plants : it is also the colouring matter of butter. Carotene is not identical with *Vitamin A* but is able to replace it in a diet. (See also p. 752.)

II. HALOGEN DERIVATIVES OF THE HYDROCARBONS

The halogen substitution products result from the replacement of hydrogen in the hydrocarbons by the halogens. The number N of substitution products derived from the normal saturated hydrocarbons, containing an even number of n carbon atoms, can be calculated by the formula :

$$*\,N = 8 \times 3^{n-2} + 2 \times 3^{\frac{n-2}{2}}$$

and when n is odd :

$$*\,N = 8 \times 3^{n-2} + 2 \times 3^{\frac{n-1}{2}}.$$

in which the unsubstituted hydrocarbon itself is counted.

If $n = 2$, then $N = 10$; if $n = 3$, then $N = 30$; if $n = 4$, then $N = 78$;
$n = 5$ $N = 234$ $n = 6$ $N = 666$ $n = 7$ $N = 1998$.

Thus nine chlorine substitution products can be derived from ethane.

General methods of preparation of the Halogen Derivatives

(1) *Formation by the direct substitution of the saturated hydrocarbons.* It was emphasized in the case of methane (p. 93) and ethane that these hydrocarbons, usually so very stable, were attacked by chlorine. A molecule of hydrogen chloride is produced for every hydrogen atom replaced by chlorine, until the entire hydrogen content is substituted. Methane, CH_4, yields finally tetra- or perchloromethane, CCl_4, whilst ethane gives hexa- or perchloroethane, C_2Cl_6.

The action of free chlorine on the paraffins is accelerated by sunlight, as is the case when it acts on free hydrogen ; by the so-called chlorine carriers, such as iodine, which exerts its influence by the formation and decomposition of ICl_3 ; by the similar behaviour of $SbCl_5$ which decomposes by heat into $SbCl_3$ and Cl_2 ; and by $AlCl_3$ (C. 1900, II. 720), etc. In very energetic chlorination the carbon

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* For these formulæ, the author's thanks are due to Herr Geheimrath A. von Baeyer of Munich.

chain is ruptured (Ber. **8**, 1296 : **10**, 801). To avoid more extreme decomposition, it is desirable to carry out the chlorination under diminished pressure (C. 1913, II. 1631, 2013).

The final products are CCl_4 and hexa- or perchlorobenzene, C_6Cl_6, with perchloroethane, C_2Cl_6, and perchloromesole, C_4Cl_6, as intermediate products (Ber. **24**, 1011).

The substituting action of bromine may be accelerated by heat, sunlight, or $AlBr_3$ (C. 1900, II. 720).

Iron is an excellent carrier of chlorine, bromine and iodine. Its action seems to be due to the formation and decomposition of ferric halides (Ann. **225**, 196 : **231**, 158). When it is used as a bromine carrier, every normal hydrocarbon passes into that bromide which contains as many bromine atoms as it has carbon atoms (Ber. **26**, 2436) ; a bromine atom attaches itself to each carbon atom.

Usually iodine does not substitute directly, inasmuch as the final iodo products undergo reduction through the hydriodic acid formed simultaneously with them :

$$C_3H_7I + HI = C_3H_3 + I_2.$$

In the presence of substances capable of uniting or decomposing HI (such as HIO_3 and HgO), iodine frequently effects substitution :

$$5C_3H_8 + 2I_2 + HIO_3 = 5C_3H_7I + 3H_2O$$
$$2C_3H_8 + 2I_2 + HgO = 2C_3H_7I + H_2O + HgI_2.$$

In direct substitution a mixture of mono- and poly-substitution products generally results, and these are separated by fractional distillation or crystallization. The attack of chlorine on a long paraffin chain, *e.g.* *n*-hexane, is directed against the CH_2 groups before the CH_3 (Ber. **39**, 2138).

(2) Mono- and polychloroparaffins can be converted into mono- and polybromoparaffins by means of $AlBr_3$ (C. 1901, I. 878). Among the bromoparaffins the bromine can be replaced partially by fluorine by means of SbF_3 (C. 1899, II. 281 : 1901, II. 804). Boiling with an alcoholic solution of an alkali iodide causes a partial replacement of the halogens in the chloro- or bromo-paraffins (Ber. **39**, 1951).

(3) The unsaturated aliphatic hydrocarbons, the olefines (p. 101), and acetylenes (p. 108), unite with hydrochloric, hydrobromic, and, especially easily, hydriodic acid. The halogen acids can be used in a glacial acetic acid (Ber. **11**, 1221), or concentrated aqueous solution.

(4) The free halogens are still more easily absorbed than their acids.

Two further reactions, already indicated above, bring about halogen substitution products from aliphatic bodies containing oxygen:

(5) Substitution of the hydroxyl group in alcohols by fluorine, chlorine, bromine, and iodine by means of their halogen acids, or their compounds with phosphorus.

(6) Action of phosphorus pentachloride, phosphorus chlorobromide, and phosphorus pentabromide, on aldehydes and ketones.

These last methods of formation will be more thoroughly discussed under the individual groups of halogen substitution products.

Reactions of the Halogen Derivatives

The reactions which take place among the halogen-paraffin compounds have been referred to under mode of formation (2). The iodine derivatives are the most unstable. In the light they rapidly acquire a red colour, with the separation of iodine. The chlorides and bromides, rich in hydrogen, burn with a green-edged flame (p. 10).

(1) Nascent hydrogen (zinc and hydrochloric acid or glacial acetic acid, sodium amalgam and water) can reconvert all the halogen

derivatives, by successive removal of the halogen atoms, into the corresponding hydrocarbons :

$$CHCl_3 + 3H_2 = CH_4 + 3HCl.$$

(2) Alcoholic sodium and potassium hydroxides cause the separation of halogen acid, and the production of unsaturated compounds (p. 102) :

$$\underset{\text{Propyl bromide.}}{CH_3{\cdot}CH_2{\cdot}CH_2Br} + KOH = \underset{\text{Propylene.}}{CH_3{\cdot}CH : CH_2} + KBr + H_2O.$$

In this reaction the halogen carries away with it the hydrogen of the least hydrogenated adjacent carbon atom (comp. p. 106). Such a decomposition sometimes occurs on application of heat, and is favoured by the presence of anhydrous metallic chlorides (C. 1905, II. 750).

Many other reactions of the haloid compounds will be discussed later.

A. HALOGEN PARAFFINS

1. Monohalogen Paraffins. Alkyl Halides

$C_nH_{2n+1}X.$

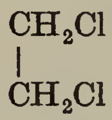
The alkyl halides can be regarded as derived from the halogen hydrides by replacement of hydrogen by an alkyl group :

$H{\cdot}Cl$	$H{\cdot}Br$
$C_2H_5{\cdot}Cl$	$CH_3{\cdot}Br$
Ethyl chloride (Chloroethane).	Methyl bromide (Bromomethane)

On account of their close relationship to the monohydric alcohols, which are the alkyl hydroxides, they are discussed later as " Haloid Esters of the alcohols."

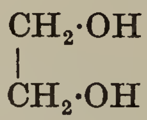
2. Dihalogen Paraffins, $C_nH_{2n}X_2$

(*a*) Dihalogen paraffins, where two halogen atoms are attached to two different carbon atoms, may be viewed similarly as the haloid esters of dihydric paraffin alcohols or glycols. They can be derived from these and will be considered together with them :



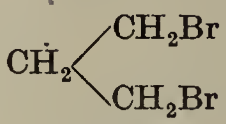
$$\begin{array}{c}CH_2Cl\\ |\\ CH_2Cl\end{array}$$

Ethylene chloride.

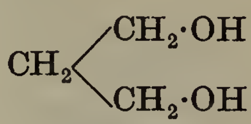


$$\begin{array}{c}CH_2{\cdot}OH\\ |\\ CH_2{\cdot}OH\end{array}$$

Ethylene glycol.

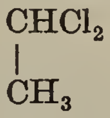


Trimethylene bromide.



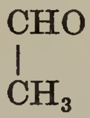
Trimethylene glycol.

(*b*) Dihalogen paraffins, the two halogen atoms of which are attached to the same carbon atom, can be obtained from the aldehydes and ketones by means of phosphorus halides. They will, therefore, be discussed after the aldehydes and the ketones :



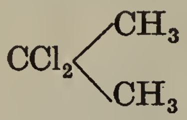
$$\begin{array}{c}CHCl_2\\ |\\ CH_3\end{array}$$

Ethylidene chloride.

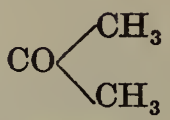


$$\begin{array}{c}CHO\\ |\\ CH_3\end{array}$$

Acetaldehyde.



β-Dichloropropane.



Acetone.

It should be remarked here that the unsymmetric ethane dihalides —*e.g.* $CH_3{\cdot}CHCl_2$, ethylidene chloride—have lower boiling points and lower specific gravities than the corresponding symmetric isomers —*e.g.* ethylene chloride, $CH_2Cl{\cdot}CH_2Cl$.

3. Polyhalogen Paraffins

The polyhalogen paraffins, containing but one halogen atom to each carbon atom, will be discussed after the corresponding polyhydric paraffin alcohols.

The simplest and most important representatives of the paraffin trihalides, in which three halogen atoms are attached to the same carbon atom, are the trihalogenmethanes :

CHF_3	$CHCl_3$	$CHBr_3$	CHI_3
Fluoroform.	Chloroform.	Bromoform.	Iodoform.

They are so intimately related to formic acid and its derivatives that they will be considered after this acid.

The most important tetrahalogen derivatives are the carbon tetrahalides. They bear the same relation to carbonic acid that the methane trihalides do to formic acid. They will, therefore, be treated after carbonic acid :

CF_4	CCl_4	CBr_4	CI_4
Carbon tetrafluoride.	Carbon tetrachloride.	Carbon tetrabromide.	Carbon tetraiodide.

These compounds are also called methane perhalides, to indicate that the hydrogen in them is completely replaced by halogens.

Polyhalogen Ethanes.—The following table contains the boiling points of the known polychloro- and polybromo-ethanes :

Name.	Formula.	M.P.	B.P.	Formula.	M.P.	B.P.
ααβ-Trichloroethane . Ethenyl Trichloride .	CH_2Cl $\dot{C}HCl_2$	—	114°	$CHBr_2$ $\dot{C}H_2Br$	—	187–188°
ααα-Trichloroethane . Methyl Chloroform .	CCl_3 $\dot{C}H_3$	—	74·5°	—	—	—
sym-Tetrachloroethane .	$CHCl_2$ $\dot{C}HCl_2$	—	147°	$CHBr_2$ $\dot{C}HBr_2$	—	102° (12 mm.)
as-Tetrachloroethane .	CCl_3 $\dot{C}H_2Cl$	—	129°	CBr_3 $\dot{C}H_2Br$	—	105° (13·5 mm.)
Pentachloroethane . .	CCl_3 $\dot{C}HCl_2$	—	159°	CBr_3 $\dot{C}HBr_2$	54°	decomposes
Hexachloroethane . . Perchloroethane . . .	CCl_3 $\dot{C}Cl_3$	187°	sublimes	CBr_3 $\dot{C}Br_3$	—	decomposes at 200–210° without melting.

For the relations existing between the boiling points and specific volumes of the halogen substitution products of the ethanes, see Ber. **15**, 2559. As to the refractive power of the brominated ethanes, see Z. physik. Chem. **2**, 236.

The polychloro- and polybromo-ethanes have few genetic relationships with the oxygen compounds corresponding with them. The methods of formation and the reactions of the polysubstituted ethanes are most intimately related to the methods of formation and the reactions of the halogen substitution products of the ethylenes and acetylenes, which are described in the following pages.

It may be merely mentioned here that by the action of chlorine on ethyl chloride and ethylidene chloride in sunlight methyl chloroform or α-trichloroethane, CH_3CCl_3, is produced, together with ααβ-trichloroethane, $CH_2Cl{\cdot}CHCl_2$ (J. pr. Chem. [2], **80**, 305). The further action of chlorine on the trichloroethanes produces $CH_2Cl{\cdot}CCl_3$, $CHCl_2{\cdot}CCl_3$, and perchloroethane, $CCl_3{\cdot}CCl_3$. $CHCl_2{\cdot}CHCl_2$ is formed from acetylene dichloride and chlorine, as well as from dichloroaldehyde by means of phosphorus pentachloride (Ber. **15**, 2563). Only methyl chloroform, $CH_3{\cdot}CCl_3$, related to acetic acid in the same way as chloroform is to formic acid, will be further described, together with the chlorides of the fatty acids.

Acetylene tetrachloride, *sym.*- **Tetrachloroethane,** $CHCl_2{\cdot}CHCl_2$, is prepared by the direct union of acetylene and chlorine (p. 113). The gases combine quietly when they are led separately into boiling water, or when sulphur chloride is alternately saturated with chlorine and acetylene in presence of iron powder (C. 1905, I. 1585 : 1906, II. 746).

The addition of chlorine to acetylene is conveniently carried out by treating the addition product of acetylene with antimony pentachloride alternately with chlorine and acetylene (C. 1904, II. 1177 : 1908, I. 1504). *s*-Tetrachloroethane is also formed by the action of phosphorus pentachloride on dichloroacetaldehyde, $CHCl_2{\cdot}CHO$. It is used technically as a solvent, and for the preparation of other polychloro- derivatives of ethane and ethylene (Chem. Ztg. **35**, 1053).

Pentachloroethane, b.p. 159°, is obtained by the addition of chlorine to trichloroethylene.

Perchloroethane, C_2Cl_6, m.p. 187°, b.p. 185·5°/777 mm., D = 2·01, results, together with perchlorobenzene (Z. Electrochem. **8**, 165), from the direct union of carbon and chlorine when an electric arc is struck in an atmosphere of chlorine. A good yield is obtained when carbon tetrachloride is warmed with amalgamated aluminium (Ber. **38**, 3058). It forms a crystalline mass, with a camphor-like odour. It sublimes at the ordinary pressure, as its critical pressure lies below 760 mm. When its vapours are conducted through a tube heated to redness it breaks down into Cl_2 and perchloroethylene. It yields the latter compound when it is treated with potassium sulphide.

α-Tribromoethane, $CH_3{\cdot}CBr_3$, has not yet been prepared.

Acetylene Tetrabromide, $CHBr_2{\cdot}CHBr_2$, is obtained from acetylene and bromine. Zinc dust and alcohol convert it into acetylene dibromide (Ann. **221**, 141), whilst benzene and $AlCl_3$ change it into anthracene (*q.v.* Vol. II.).

Hexabromoethane, C_2Br_6, is obtained by the addition of bromine to acetylene tetrabromide in the presence of aluminium bromide (C. 1898, I. 882). It is a colourless, crystalline compound, dissolving with difficulty in alcohol and ether. It breaks down at 200° into bromine and perbromoethylene, $CrBr_4$.

Propane derivatives.—A series of chloro-substituted propanes have been obtained by the condensation of polychloroethylenes with chloroform or carbon tetrachloride in the presence of aluminium chloride (J. pr. Chem. [2] **89**, 414), *e.g.* :

$$CCl_2 : CHCl + CHCl_3 \xrightarrow{\qquad} CHCl_2{\cdot}CHCl{\cdot}CCl_3.$$

The most important of the polyhalogen propanes are the compounds derived from glycerol, of the general formula $CH_3X{\cdot}CHX{\cdot}CH_2X$, where X represents a halogen atom. They are discussed later, after glycerol.

Mixed Halogen Substitution Products of the Paraffins.—There are numerous paraffins containing different halogens side by side in the same molecule.

B. HALOGEN DERIVATIVES OF THE OLEFINES

As a general rule, the halogen substitution products of the unsaturated hydrocarbons cannot be prepared by direct action of the halogens, since addition products are apt to result (p. 106). They are produced, however, by the moderated action of alcoholic potassium hydroxide (C. 1901, I. 816 : II. 804), or Ag_2O, on the disubstituted hydrocarbons $C_nH_{2n}X_2$. This reaction occurs very readily if the addition products of the olefines are employed :

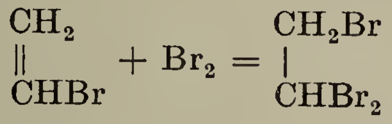
$$\underset{\substack{\text{Ethylene}\\ \text{chloride.}}}{C_2H_4Cl_2} + KOH = \underset{\substack{\text{Monochloro-}\\ \text{ethylene.}}}{C_2H_3Cl} + KCl + H_2O.$$

When the alcoholic potassium hydroxide acts very energetically, the hydrocarbons of the acetylene series are formed.

When heated with zinc or iron turnings in presence of water, the polyhalogen ethanes are converted into halogen ethylenes (C. 1909, II. 2103 : 1910, I. 700).

$$CHCl_2{\cdot}CHCl_2 + Zn \longrightarrow CHCl : CHCl + ZnCl_2$$

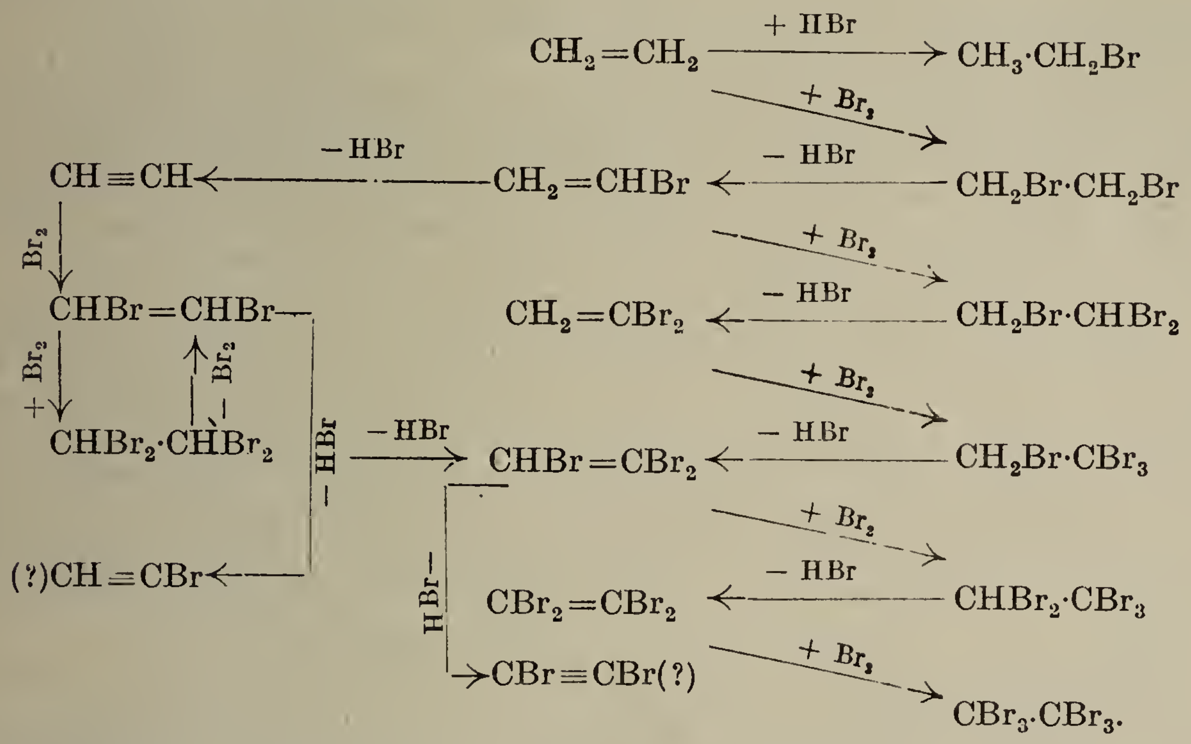
Being unsaturated compounds they unite directly with the halogens, and also with the halogen acids :



$$\begin{matrix} CH_2 \\ \| \\ CHBr \end{matrix} + Br_2 = \begin{matrix} CH_2Br \\ | \\ CHBr_2 \end{matrix}$$

These reactions indicate that ethylene is the parent substance for the preparation of nearly all the halogen-substituted ethanes and ethylenes, as well as for the preparation of acetylene.

The following diagram represents how, by the addition of bromine and the loss of hydrogen bromide, the bromine substitution derivatives of the ethanes are connected with ethylene, with the ethylene bromine derivatives, and with acetylene (Ann. **221**, 156) :



Monohalogenethylenes, *Vinyl Chloride,* $CH_2{=}CHCl$, and *Vinyl Bromide,* $CH_2{=}CHBr$, are obtained from ethylene chloride and ethylene bromide by the action of alcoholic potassium hydroxide, which, by continued action on them, produces acetylene. The group $CH_2{=}CH-$ is called vinyl. Vinyl chloride can also be obtained by heating ethylene dichloride or ethylidene dichloride (Ber. **35**, 3524). More recently it has been obtained by the action of acetylene on concentrated hydrochloric acid in the presence of metallic salts (Brit. Pat. 156120 : J.C.S. **122**, 517).

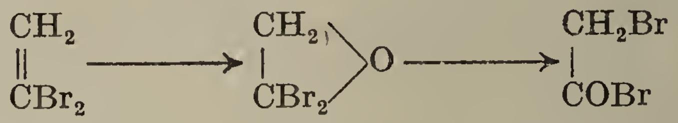
s-**Dihalogenethylenes.**—The *s*-dihalogen ethylenes occur in two readily interconvertible stereoisomeric forms. The removal of halogen hydride takes place appreciably more rapidly under the action of alcoholic potash from the *cis-* compounds than from the *trans-* isomerides (Bull. Soc. Chim. Belg. **27**, 209 : **28**, 234 : Compt. rend. **158**, 1582 : Chem. Ztg. **37**, 622).

The *dichloro-* and *dibromo-* compounds are obtained by the direct union of the halogen and acetylene, when the latter is present in great excess (Ann. **178**, 116 : C. 1913, II. 1178). They are more readily obtained from the tetrahalogen ethanes by removal of halogen by zinc or iron turnings. The *diiodo*-compound is obtained by passing acetylene over heated iodine (C. 1899, I. 966). The configuration of the iodo compounds has been established by converting them into the cyanides ; hydrolysis of these gives the dibasic maleic and fumaric acids, the liquid iodo compound yielding maleic acid (*cis*) and the solid, fumaric acid (*trans*) :

	Cis- form.	*Trans*- form.
s-Dichloroethylene, CHCl : CHCl .	b.p. 60·2°	m.p. 48·5°
s-Dibromoethylene CHBr : CHBr .	b.p. 112°	b.p. 108°
s-Diiodoethylene CHI : CHI . .	b.p. 188°	m.p. 73° : b.p. 191°.

Chlorine combines with diiodoethylene and chloroiodoethylene to form the unstable iodochlorides, $CHCl : CHICl_2$, m.p. 75°, and $CHI : CHICl_2$ dec. 37°, which like the aromatic iodochlorides can be converted into iodoso-, iodoxy- and iodonium compounds (Ann. **369**, 131).

as-**Dihalogenethylenes.** *αα-Dichloroethylene*, $CH_2 : CCl_2$, b.p. 37°, and the *αα-dibromo-* compound, b.p. 91°, are obtained from the ααβ-trihalogenethanes by removal of halogen acid. Like the monohalogenethylenes they show a great tendency to polymerization (Ber. **12**, 2076 : C. 1912, I. 1980). The dibromo-compound undergoes autoxidation to form bromoacetyl bromide, probably with intermediate ethylene oxide formation, according to the scheme :



αα-Chlorobromoethylene similarly yields a mixture of chloroacetyl bromide and bromoacetyl chloride.

Trichloroethylene.—$CHCl : CCl_2$, b.p. 88°, is obtained from *s*-tetrachloroethane by heating with milk of lime (C. 1906, II. 571). By autoxidation it yields dichloroacetyl chloride, but a simultaneous decomposition to phosgene ($COCl_2$), carbon monoxide and hydrogen chloride takes place (J. pr. Chem. [2] **85**, 78). Treatment with sodium ethoxide gives the very reactive dichlorovinyl ethyl ether (*q.v.* See also C. 1910, I. 308). The *tribromo-* compound, b.p. 164°, also autoxidizes to dibromoacetyl bromide.

Tetrachloroethylene (*Perchloroethylene*), $CCl_2 : CCl_2$, b.p. 121°, is obtained from pentachloroethane by removal of hydrogen chloride. Like di- and trichloroethylenes, it is used as a solvent for fats, resins, etc. Treatment with ozonized air gives a mixture of phosgene and trichloroacetyl chloride (Ber. **27**, R. 509 : C. 1899, I. 588). *Tetrabromoethylene* melts at 57°. (For boiling-point relationships between bromoethylenes and bromoethanes, see Ann. **221**, 156.) *Tetraiodoethylene*, m.p. 187°, is obtained together with the diiodo compound by the action of iodine and water on calcium carbide (Ber. **26**, R. 289 : **30**, 1200 : **38**, 237).

Fluoroethylenes.—See Bull. Acad. roy. Belg. **1901**, 383.

Halogen Derivatives of Propylene.—There are three isomers of the monohalogen propylenes.

(1) *α-derivatives*, $CH_3{\cdot}CH : CHX$, which are obtained from the propylidene halides, $CH_2{\cdot}CH_2CHX_2$, by heating with alcoholic potassium hydroxide. The propylidene derivatives are obtained from propaldehyde and phosphorus pentahalides.

(2) *β-derivatives*, $CH_3{\cdot}CX : CH_2$, are obtained similarly from the dihalogen derivatives, $CH_3{\cdot}CX_2{\cdot}CH_3$, of acetone.

(3) *γ-derivatives*, $CH_2X{\cdot}CH : CH_2$.—These are the *allyl* halides derived from allyl alcohol, and are described later among the alkyl halides.

C. HALOGEN DERIVATIVES OF ACETYLENES

Chloroacetylene, CCl ⋮ CH, was first obtained from dichloroacrylic acid, $CCl_2 : CH{\cdot}CO_2H$ and barium hydroxide (Ann. **203**, 88 : Ber. **23**, 3783). It is also obtained from *s*-dichloroethylene by warming with alcoholic potash. It is a poisonous gas which is spontaneously inflammable and explosive in air. With ammoniacal silver and copper solutions it yields very explosive precipitates. Alkaline mercuric cyanide solution yields the compound $Hg(C \vdots CCl)_2$, which is also obtained from *s*-dichloroethylene and mercuric cyanide. This compound is decomposed on warming with potassium cyanide to form pure chloroacetylene. By passing chloroacetylene into aqueous mercuric chloride solution, the compound $(ClHg)_3C{\cdot}CO_2H$, trichloromercuriacetic acid, is formed as a white precipitate (Ber. **42**, 4232).

Acetylene and other compounds containing hydrogen replaceable by metals are readily halogenated by halogens in presence of excess alkali, *e.g.* **Dichloroacetylene,** b.p. 32–33°, is obtained by the action of acetylene on an alkaline potassium hypochlorite solution in an atmosphere of nitrogen (Ber. 1930, **63**, 1868).

Bromoacetylene is similar in its reactions to chloroacetylene.

Dibromoacetylene, $CBr \vdots CBr$, b.p. 77°, D 2·0 is obtained from tribromoethylene and alcoholic potash. It is spontaneously inflammable (C. 1903, II. 531 : 1907, I. 231).

Diiodoacetylene, m.p. 81° with decomposition, is obtained by the action of iodine on silver acetylide or calcium carbide, or of iodine and alkali hypoiodite on acetylene (Ber. **37**, 4415 : C. 1911, II. 1814), or from barium iodopropiolate by heating with water (Ann. **308**, 326 : Ber. **34**, 2718). In the light or on heating it decomposes with formation on tetraiodoethylene and carbon (Ber. **37**, 3453).

Nef regarded these very poisonous and labile compounds as derivatives of the hypothetical acetylidene, $CH_2 : C$, and likened them to hydrogen cyanide and the *iso*nitriles (Ann. **298**, 332 : *cf.* C. 1907, I. 231 : Ber. **46**, 143).

The halogenacetylenes polymerize much more readily than acetylene itself, and the products, in part, are benzene derivatives ; *e.g.* bromoacetylene gives tribromobenzene.

$$3CH \vdots CBr \longrightarrow C_6H_3Br_3$$

Iodoallylene, $CH_3C \vdots CI$, b.p. 110°, is obtained from silver allylide and iodine solutions (Ann. **308**, 309).

“ **Perchloromesole,**” C_4Cl_6, probably $CCl_2 : CCl{\cdot}CCl : CCl_2$ (C. 1913, II. 99), is frequently obtained as an end product in “ exhaustive chlorinations ” (Ber. **10**, 804 : *cf.* Ber. **22**, 1269).

OXYGEN-CONTAINING DERIVATIVES OF THE ALIPHATIC HYDROCARBONS

The oxygen-containing derivatives can be considered as derived from the hydrocarbons by the replacement of hydrogen atoms by hydroxyl groups (·OH groups). When one hydroxyl group is introduced, *monohydric* alcohols are produced :

$$CH_3{\cdot}CH_3 \longrightarrow CH_3{\cdot}CH_2OH.$$

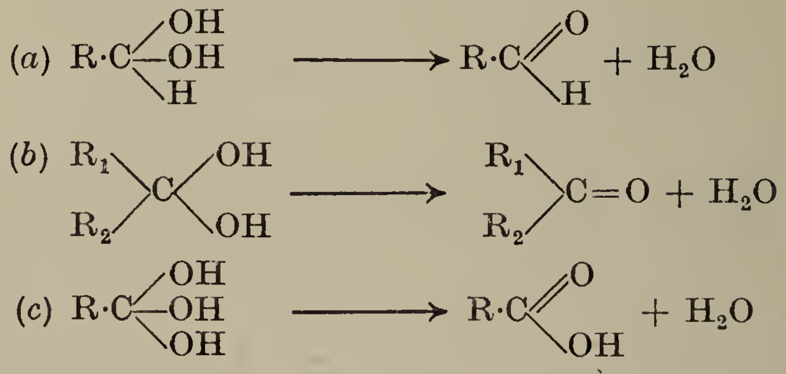
More than one hydroxyl group may be introduced, each being attached to a different carbon atom. This leads to the formation of further series of alcohols, which are distinguished as monohydric, di-, tri-, and poly-hydric alcohols according to the number of hydroxyl groups they contain. The simplest alcohol of each series contains as many carbon atoms as it has hydroxyl groups.

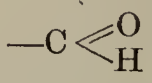
$CH_3{\cdot}OH$ Methyl alcohol (the simplest monohydric alcohol)
$CH_2OH{\cdot}CH_2OH$ Ethylene glycol (the simplest dihydric alcohol)
$CH_2OH{\cdot}CHOH{\cdot}CH_2OH$ Glycerol (the simplest trihydric alcohol)

and similarly erythritol, arabitol, mannitol containing respectively four, five and six hydroxyl groups and four, five and six carbon atoms, are the simplest representatives of the tetra-, penta and hexahydric alcohols.

Further, more than one hydrogen atom attached to the same carbon atom may be replaced by —OH groups. In such cases, with very few exceptions, water is split off from the resulting compound, and the oxygen becomes linked to carbon by a double bond.

The following possibilities have to be considered. (*a*) Two hydrogen atoms of a terminal CH_3 group are replaced, (*b*) two hydrogen atoms of an intermediate CH_2 group, and (*c*) three hydrogen atoms of a terminal CH_3 group are replaced by an equal number of hydroxyl groups. In each case water is split off, and three new classes of oxygen containing compounds are produced.



(*a*) Compounds containing the group  $-\mathrm{C}{<}^{\mathrm{O}}_{\mathrm{H}}$ are known as *Aldehydes,* where the group —CHO is called the aldehyde group.

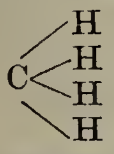
(*b*) Compounds containing the group $=\mathrm{C}=\mathrm{O}$ in union with two carbon atoms are called Ketones. The group $=\mathrm{CO}$ is known as the keto- or ketone group.

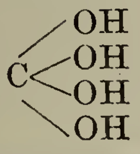
(*c*) Compounds containing the group $-\mathrm{C}\!<^{\mathrm{O}-\mathrm{H}}_{\mathrm{O}}$ are named Carboxylic acids, and the group —COOH is called carboxyl. The alcohols, aldehydes, and ketones are neutral substances. The carboxylic acids are acids, and form salts in the same manner as the mineral acids.

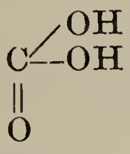
Aldehydes, ketones, and carboxylic acids as the oxidation products of alcohols, will be discussed after them. Unsaturated hydrocarbons similarly yield unsaturated alcohols, aldehydes, ketones, and carboxylic acids. In the following sections the unsaturated derivatives will receive attention after the saturated compounds corresponding with them; *i.e.* the unsaturated alcohols will follow the saturated alcohols.

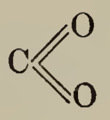
Similarly, an almost endless series of oxidation products is derived from the di, tri-, and poly-hydric alcohols. These compounds contain the same oxygen-containing atomic groups, as the monohydric alcohols and their oxidation products, but possess several of them in the same molecule.

Finally, when in methane, the four hydrogen atoms are replaced by hydroxyl groups, the loss of two molecules of water would be possible, and carbon dioxide, the anhydride of two acids incapable of free existence (orthocarbonic acid and ordinary metacarbonic acid) would be obtained. The carbonates are derived from the meta-acid.


Methane.


Orthocarbonic acid.


Metacarbonic acid.


Carbon dioxide.

The carbonates are salts of a dibasic acid. Therefore, carbonic acid, with its numerous derivatives, will be discussed before the dicarboxylic acids, the final oxidation products of the dihydric alcohols or glycols, whose simplest representative is oxalic acid.

III. THE MONOHYDRIC ALCOHOLS AND THEIR OXIDATION PRODUCTS

1. MONOHYDRIC ALCOHOLS

The monohydric alcohols can be looked upon as derived from water by replacement of one hydrogen atom by a monovalent alkyl group. If both hydrogen atoms in water are so substituted, there result the ethers, which are at the same time alkyl oxides or alcoholic anhydrides.

$\mathrm{H{\cdot}O{\cdot}H}$	$\mathrm{C_2H_5{\cdot}O{\cdot}H}$	$\mathrm{C_2H_5{\cdot}O{\cdot}C_2H_5}$
Water.	Ethyl alcohol.	Ethyl ether.

The monohydric alcohols contain one hydroxyl group, ·OH; bivalent oxygen links the univalent alkyl radical to hydrogen, as in

$CH_3\cdot O\cdot H$, methyl alcohol. This hydrogen atom is characterized by its ability to be exchanged for acid residues, forming compound ethers or esters, corresponding with the salts of mineral acids :

$$\underset{\text{Ethyl alcohol.}}{C_2H_5\cdot OH} + NO_2\cdot OH = \underset{\text{Ethyl nitrate.}}{C_2H_5\cdot O\cdot NO_2} + H_2O$$

Alkyls and metals can also replace the hydrogen in the alcoholic hydroxyl group :

$$\underset{\text{Methyl ethyl ether.}}{C_2H_5\cdot O\cdot CH_3} \qquad \underset{\text{Sodium ethoxide.}}{C_2H_5\cdot ONa}$$

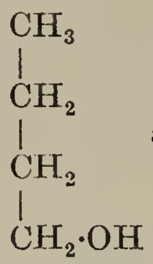
Structure of the Monohydric Alcohols.—The possible isomeric alcohols may be readily derived from the hydrocarbons. There is one possible structure for the first two members of the normal alcohols :

$$\underset{\text{Methyl alcohol.}}{CH_3\cdot OH} \qquad \underset{\text{Ethyl alcohol.}}{C_2H_5\cdot OH}$$

Two isomers can be obtained from propane, $C_3H_8 = CH_3\cdot CH_2\cdot CH_3$:

$$\underset{\text{Propyl alcohol.}}{CH_3\cdot CH_2\cdot CH_2\cdot OH} \quad \text{and} \quad \underset{\textit{iso}\text{Propyl alcohol.}}{CH_3\cdot CH(OH)\cdot CH_3}$$

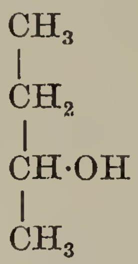
Two isomeric alcohols may be obtained from each of the isomeric butanes (p. 35) :



$$\begin{array}{c}CH_3\\|\\CH_2\\|\\CH_2\\|\\CH_2\cdot OH\end{array}$$

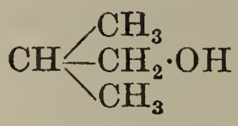
Normal butyl alcohol.

and



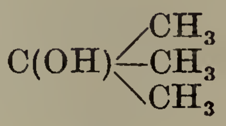
$$\begin{array}{c}CH_3\\|\\CH_2\\|\\CH\cdot OH\\|\\CH_3\end{array}$$

Secondary butyl alcohol.



*iso*Butyl alcohol.

and



tert.-Butyl alcohol.

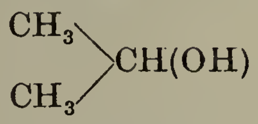
An excellent method of formulating the alcohols was introduced by Kolbe in 1860 (Ann. **113**, 307 : **132**, 102). He regarded all alcohols as derivatives of methyl alcohol, for which he proposed the name *carbinol*, and compared the alcohols, formed by the replacement of hydrogen not in union with oxygen by alcohol radicals, with the primary, secondary, and tertiary amines, resulting from the replacement of the hydrogen in ammonia by alcohol radicals. With this view as a basis, Kolbe predicted the existence of secondary and tertiary alcohols. Their first representative was discovered shortly afterwards. By the replacement of one hydrogen atom in carbinol by an alkyl group the primary alcohols result :

$$\underset{\substack{\text{Methyl carbinol, or}\\ \text{Ethyl alcohol.}}}{CH_3\cdot CH_2OH} \qquad \underset{\substack{\text{Ethyl carbinol, or}\\ \text{Propyl alcohol.}}}{C_2H_5\cdot CH_2OH}$$

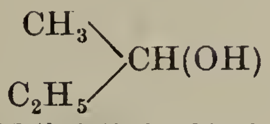
If the replacing group possesses an unbranched carbon chain, the primary alcohols are said to be *normal*. In alcohols of this class the carbon atom carrying the hydroxyl group has two hydrogen atoms (they contain the group $—CH_2\cdot OH$). Hence compounds of this variety can easily pass into aldehydes (containing the CHO group) and acids (with COOH group) on oxidation (see p. 224) :

$$\underset{\text{Primary alcohol.}}{R\cdot CH_2OH} \quad \text{yields} \quad \underset{\text{Aldehyde.}}{R\cdot CHO} \quad \text{and} \quad \underset{\text{Acid.}}{R\cdot COOH}$$

The *secondary alcohols* result when two hydrogen atoms in carbinol, $CH_3{\cdot}OH$, are replaced by alkyl groups :

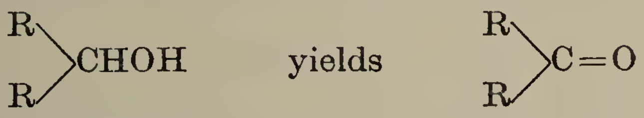

$\begin{matrix}CH_3\\CH_3\end{matrix}\!>CH(OH)$

Dimethylcarbinol
(*iso*Propyl alcohol).


$\begin{matrix}CH_3\\C_2H_5\end{matrix}\!>CH(OH)$

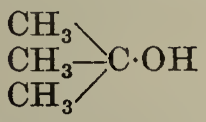
Methylethylcarbinol
(*iso*Butyl alcohol).

In alcohols of this class the carbon atom carrying the OH group has but one additional hydrogen atom ; they contain the group $>CH{\cdot}OH$. They do not furnish corresponding aldehydes and acids, but, when oxidized, they pass into ketones :


$\begin{matrix}R\\R\end{matrix}\!>CHOH \quad \text{yields} \quad \begin{matrix}R\\R\end{matrix}\!>C=O$

Secondary alcohol. Ketone.

When, finally, all three hydrogen atoms in carbinol are replaced by alkyls, there result the *tertiary alcohols*, containing the group $\geqslant C{\cdot}OH$.


$\begin{matrix}CH_3\\CH_3\\CH_3\end{matrix}\!\!-\!C{\cdot}OH$ Trimethylcarbinol.

The tertiary alcohols decompose when oxidized.

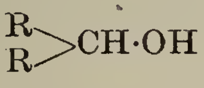
The " Geneva names " for the alcohols are derived from the names of the corresponding hydrocarbons, with the addition of the final syllable " ol " :

$CH_3{\cdot}OH$ = [Methanol] ; $CH_3{\cdot}CH_2{\cdot}OH$ = [Ethanol]:
$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}OH$ = [1-Propanol] ; $CH_3{\cdot}CHOH{\cdot}CH_3$ = [2-Propanol].

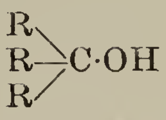
The parallelism between the formulæ of the three classes of alcohols and the three classes of amines (*q.v.*), is very evident upon studying the following general formulæ :

$R{\cdot}CH_2{\cdot}OH$

Primary alcohols.


$\begin{matrix}R\\R\end{matrix}\!>CH{\cdot}OH$

Secondary alcohols.


$\begin{matrix}R\\R\\R\end{matrix}\!\!-\!C{\cdot}OH$

Tertiary alcohols.

$R{\cdot}NH_2$

Primary amine.


$\begin{matrix}R\\R\end{matrix}\!>NH$

Secondary amine.


$\begin{matrix}R\\R\\R\end{matrix}\!\!-\!N$

Tertiary amine.

The behaviour of alcohols on oxidation is of great importance in ascertaining whether a certain alcohol is primary, secondary, or tertiary in character. What has already been stated may be summarized thus :

A *primary* alcohol on oxidation yields an *aldehyde*, which passes into a carboxylic acid if the action be continued. This acid contains as many carbon atoms in its molecule as the parent alcohol. Oxidation changes a *secondary* alcohol into a *ketone*, having an equal number of carbon atoms in its molecule. A *tertiary* alcohol breaks down on oxidation into compounds having a lower carbon content.

Formation of Alcohols.—*Summary of Reactions.*—They are obtained from bodies containing a like number of carbon atoms :

(1) By the saponification of acid esters.
(2) By the reduction of polyhydric alcohols.
(3) By the action of nitrous acid on amines.
(4) and (5) By the reduction of their oxidation products.

From nucleus-syntheses (p. 131) :

(6) and (7) By the action of magnesium alkyl halide or zinc alkyls, or zinc and alkyl iodides, on aldehydes, acid chlorides, ketones, formic esters, acetic esters, chlorinated ethers and ethylene oxide.

(1*a*) *From Haloid Esters or Alkyl Halides.*—It was mentioned, in describing the reactions of the alkyl halides, that the latter afford a means of passing from the paraffins and olefines to the alcohols (p. 120). As alkali hydroxide causes the separation of a halogen acid from the alkyl halides, it is possible to exchange hydroxyl for the halogen, especially if this be iodine. This is most easily accomplished by the action of freshly precipitated, moist silver oxide, or by heating with lead oxide and water:

$$C_2H_5I + AgOH = C_2H_5{\cdot}OH + AgI.$$

Even water alone causes a partial transposition of the more reactive tertiary alkyl iodides; the other alkyl halides in general when heated for some time with 10–15 volumes of water to 100° are completely converted into alcohols (Ann. **186**, 390).

Tertiary alkyl iodides heated to 100° with methyl alcohol pass into alcohols and methyl iodide (Ann. **220**, 158).

(1*b*) *By the Saponification of their Esters.*—It is often more practical first to convert the halogen derivatives into acetic acid esters, by heating with silver or potassium acetate:

$$\underset{}{C_2H_5Br} + \underset{\text{Potassium acetate.}}{CH_3{\cdot}COOK} = \underset{\text{Ethyl acetate.}}{CH_3{\cdot}COOC_2H_5} + KBr$$

and then to boil these with potassium or sodium hydroxide, to obtain the alcohols:

$$CH_3{\cdot}COOC_2H_5 + KOH = C_2H_5{\cdot}OH + CH_3COOK.$$

The second reaction is called *saponification*, because by means of it the soaps, *i.e.* the alkali salts of the fatty acids and glycerol (*q.v.*), are obtained from the glycerol esters of the fatty acids—the fats. More generally this reaction is known as *hydrolysis*.

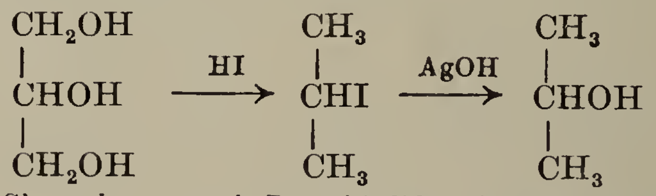
(1*c*) *From Ethyl Sulphuric Acid by boiling water.*

$$\underset{\text{Ethyl sulphuric acid.}}{C_2H_5O{\cdot}SO_3H} + H_2O = C_2H_5{\cdot}OH + H_2SO_4.$$

This reaction constitutes the transition from the olefines to the alcohols, as these esters may be easily obtained by directly combining the unsaturated hydrocarbons with sulphuric acid.

Many olefines (like *iso*- and *pseudo*-butylene) dissolve at once in dilute nitric acid, absorb water, and yield alcohols (Ann. **180**, 245).

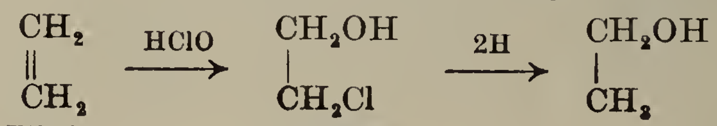
(2) *The reduction of polyhydric alcohols* by hydriodic acid yields the iodides of secondary alcohols, which are converted by methods 1*a* and 1*b* into the alcohols themselves, *e.g.*:



$$\begin{array}{c}CH_2OH\\|\\CHOH\\|\\CH_2OH\end{array}\xrightarrow{HI}\begin{array}{c}CH_3\\|\\CHI\\|\\CH_3\end{array}\xrightarrow{AgOH}\begin{array}{c}CH_3\\|\\CHOH\\|\\CH_3\end{array}$$

Glycerol. *iso*Propyl iodide. *iso*Propyl alcohol.

Or the chlorhydrins of the polyhydric alcohols may be reduced, *e.g.*:



$$\begin{array}{c}CH_2\\\|\\CH_2\end{array}\xrightarrow{HClO}\begin{array}{c}CH_2OH\\|\\CH_2Cl\end{array}\xrightarrow{2H}\begin{array}{c}CH_2OH\\|\\CH_3\end{array}$$

Ethylene. Ethylene chlorhydrin,

(3) *Action of nitrous acid on the primary amines:*

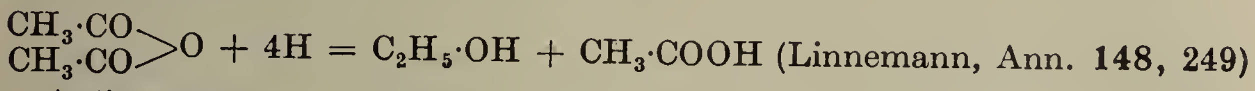
$$C_2H_5NH_2 + NO{\cdot}OH = C_2H_5{\cdot}OH + N_2 + H_2O.$$

In the case of the higher alkylamines transpositions often occur, and instead of the primary alcohols, there result secondary alcohols (Ber. **16**, 744).

(4) Primary alcohols result from the *reduction of* (*a*) *aldehydes*, (*b*) *acid chlorides*, and (*c*) *acid anhydrides*; also, by reduction of (*d*) *acid esters* by means of sodium and alcohol; *acid amides* yield primary amines as well as primary alcohols by this reaction (C. 1904, I. 577: II. 1697).

(*a*) $C_2H_5{\cdot}CHO + 2H = CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}OH$ (Würtz, Ann. **123**, 140).
Propyl aldehyde.

(*b*) $CH_3{\cdot}COCl + 4H = CH_3{\cdot}CH_2{\cdot}OH + HCl.$
Acetyl chloride.

(*c*)


$$\begin{matrix}CH_3{\cdot}CO\\ CH_3{\cdot}CO\end{matrix}\!\!>\!O + 4H = C_2H_5{\cdot}OH + CH_3{\cdot}COOH$$ (Linnemann, Ann. **148**, 249)

Acetic anhydride.

Aldehydes are first formed in the reduction of acid chlorides and anhydrides; they in turn are reduced to alcohols. As reducing agents, dilute sulphuric acid or acetic acid, together with sodium amalgam, sodium, iron filings, and zinc dust may be employed (Ber. **9**, 1312: **16**, 1715).

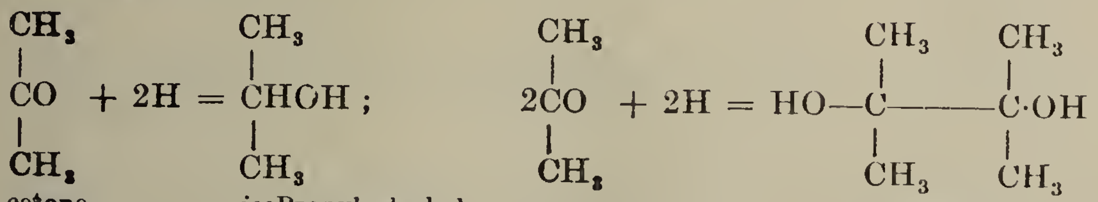
The last of these reactions is that by which an alcohol can be converted into another containing an atom more of carbon. The alcohol is changed through the iodide to the cyanide, and the latter to the acid, which, by reduction of its chloride or its aldehyde, yields the new alcohol:

$$\begin{tikzcd} CH_3OH \arrow[r] & CH_3I \arrow[r] & CH_3CN \arrow[r] & CH_3COOH \arrow[r] & CH_3COCl \arrow[llll, bend left] \\ CH_3CH_2OH & & & & \end{tikzcd}$$

(*d*) $CH_3{\cdot}COOC_5H_{11} + 4Na + 2C_5H_{11}OH = CH_3{\cdot}CH_2{\cdot}ONa + 3C_5H_{11}ONa$
Amyl acetate.
(*Bouveault* and *Blanc*, Bull. Soc. Chim. [3], **31**, 672.)

"Sodium-ammonium" can be used in this reaction in place of sodium (Ann. chim. [9], **8**, 145). The reaction can be made almost quantitative by reducing an ethereal solution of the ester, in presence of a solution of sodium acetate as a separate lower layer at − 5°, sodium being added and the ethereal layer being kept just acid by addition of 80 per cent. acetic acid (*Prins*, Rec. trav. chim. 1923, **42**, 1050).

(5) The reduction of ketones yields secondary alcohols (*Friedel*, Ann. **124**, 324), together with pinacones (*q.v.*), the di-tertiary dihydric alcohols or glycols:



$$\begin{matrix}CH_3\\ |\\ CO\\ |\\ CH_3\end{matrix} + 2H = \begin{matrix}CH_3\\ |\\ CHOH\\ |\\ CH_3\end{matrix}; \qquad \begin{matrix}CH_3\\ |\\ 2CO\\ |\\ CH_3\end{matrix} + 2H = HO{-}\begin{matrix}CH_3\\ |\\ C\\ |\\ CH_3\end{matrix}{-}{-}\begin{matrix}CH_3\\ |\\ C{\cdot}OH\\ |\\ CH_3\end{matrix}$$

Acetone. *iso*Propyl alcohol. Pinacone.

Biochemical reduction of ketones to optically active alcohols, see Ber. **52**, 2237.

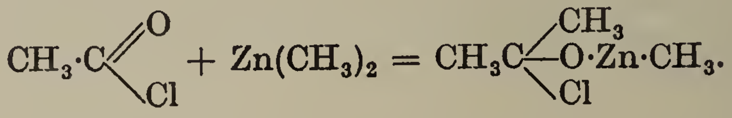
Nuclear-synthetic Methods of Formation

(6) *By means of zinc alkyls* from (*a*) acid chlorides, (*b*) ketones, (*c*) aldehydes and (*d*) esters.

(6*a*) *From Acid Chlorides.*—A very remarkable synthetic method, proposed by Butlerow (1864), which led to the discovery of the *tertiary* alcohols, consists in the action of the zinc compounds of the alkyls on the chlorides of the acid radicals (Z. Chem., 1864, 385 : 1865, 614).

The reaction proceeds in three stages. At first one molecule of zinc alkyl reacts, and forms an addition compound with the acid chloride, as a result of the breaking down of the double bond between the carbon and oxygen :

I.

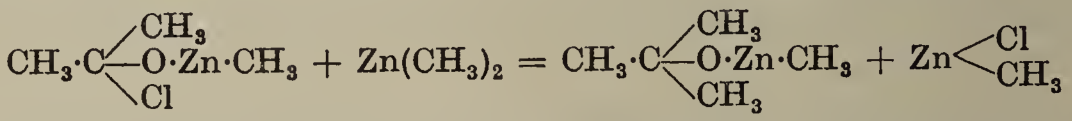


$$\mathrm{CH_3{\cdot}C}\begin{array}{l}\diagup\!\!\diagup \mathrm{O}\\ \diagdown \mathrm{Cl}\end{array} + \mathrm{Zn(CH_3)_2} = \mathrm{CH_3C}\begin{array}{l}\diagup \mathrm{CH_3}\\ -\mathrm{O{\cdot}Zn{\cdot}CH_3}.\\ \diagdown \mathrm{Cl}\end{array}$$

Acetyl chloride.

By decomposing the reaction-product with water, acetone is formed. However, should a second molecule of the zinc alkyl act upon the new compound, further reaction will take place on longer standing :

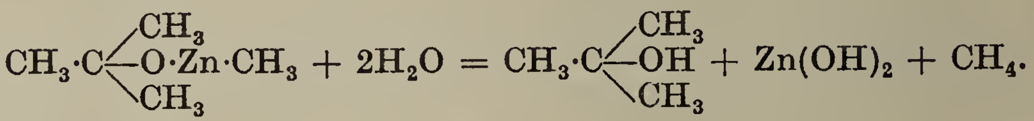
II.



$$\mathrm{CH_3{\cdot}C}\begin{array}{l}\diagup \mathrm{CH_3}\\ -\mathrm{O{\cdot}Zn{\cdot}CH_3}\\ \diagdown \mathrm{Cl}\end{array} + \mathrm{Zn(CH_3)_2} = \mathrm{CH_3{\cdot}C}\begin{array}{l}\diagup \mathrm{CH_3}\\ -\mathrm{O{\cdot}Zn{\cdot}CH_3}\\ \diagdown \mathrm{CH_3}\end{array} + \mathrm{Zn}\begin{array}{l}\diagup \mathrm{Cl}\\ \diagdown \mathrm{CH_3}\end{array}$$

If water be now permitted to react, a tertiary alcohol will be formed :

III.



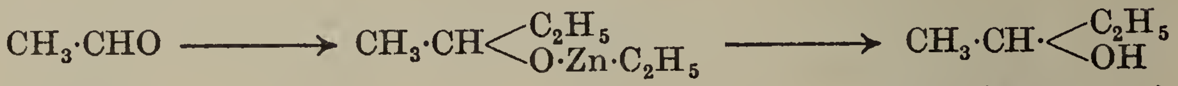
$$\mathrm{CH_3{\cdot}C}\begin{array}{l}\diagup \mathrm{CH_3}\\ -\mathrm{O{\cdot}Zn{\cdot}CH_3}\\ \diagdown \mathrm{CH_3}\end{array} + \mathrm{2H_2O} = \mathrm{CH_3{\cdot}C}\begin{array}{l}\diagup \mathrm{CH_3}\\ -\mathrm{OH}\\ \diagdown \mathrm{CH_3}\end{array} + \mathrm{Zn(OH)_2} + \mathrm{CH_4}.$$

If, in the second stage, the zinc compound of another radical be employed, the latter may be introduced, and in this manner we obtain tertiary alcohols containing two or three different alkyl groups (Ann. **175**, 374, and **188**, 110, 122 : C. 1910, II. 1201).

It is remarkable that only zinc methyl and zinc ethyl furnish tertiary alcohols, whilst zinc propyl produces only those of the secondary type with evolution of propylene (Ber. **16**, 2284 : **24**, R. 667).

(6*b*) The ketones in general do not react with the zinc alkyls. On the other hand, there are ketones which do not contain a CH_3 group united to a CO group, such as diethyl ketone $(C_2H_5)_2CO$, dipropyl ketone $(C_3H_7)_2CO$, and ethyl propyl ketone $C_2H_5{\cdot}CO{\cdot}C_3H_7$, which are converted by zinc and methyl or ethyl iodide into zinc alkyl compounds ; these, under the influence of water, pass into tertiary alcohols (Ber. **19**, 60 : **21**, R. 55). Unsaturated tertiary alcohols are obtained from all the ketones by the action of zinc and allyl iodide (Ann. **196**, 113).

(6*c*) When zinc alkyls act upon aldehydes, only one alkyl group enters the molecule, and the reaction-product of the first stage yields a *secondary* alcohol when treated with water (Ann. **213**, 369 ; and Ber. **14**, 2557) :

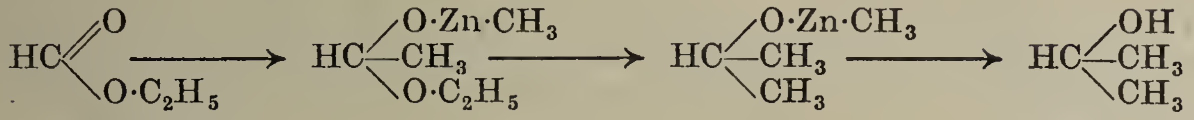


$$\mathrm{CH_3{\cdot}CHO} \longrightarrow \mathrm{CH_3{\cdot}CH}\!<\!\begin{array}{l}\mathrm{C_2H_5}\\ \mathrm{O{\cdot}Zn{\cdot}C_2H_5}\end{array} \longrightarrow \mathrm{CH_3{\cdot}CH{\cdot}}\!<\!\begin{array}{l}\mathrm{C_2H_5}\\ \mathrm{OH}\end{array}$$

Aldehyde. Methylethylcarbinol.

All aldehydes (even those with unsaturated alkyls, and also furfural) react in this way—but only with zinc methyl and zinc ethyl, whilst with the higher zinc alkyls the aldehydes undergo reduction to their corresponding alcohols (Ber. **17**, R. 318). With zinc methyl, chloral, $CCl_2{\cdot}CHO$, yields trichloro*iso*propyl alcohol, $CCl_3{\cdot}CH(OH){\cdot}CH_3$; whereas with zinc ethyl it is reduced to trichloroethyl alcohol (Ann. **223**, 162).

(6*d*) Just as tertiary alcohols are obtained from the acid chlorides, so *secondary* alcohols are derived from the esters of formic acid. Zinc alkyls (or, better, alkyl iodides and zinc), are allowed to react in this case, and two alkyls are introduced :



Ethyl formate. Dimethyl carbinol.

By using some other zinc alkyl in the second stage of the reaction, or by working with a mixture of two alkyl iodides and zinc, two different alkyl groups may also be introduced here (Ann. **175**, 362, 374).

Zinc and allyl iodide (not ethyl iodide, however) react similarly with acetic acid esters. Two alkyl groups are introduced and unsaturated tertiary alcohols formed (Ann. **185**, 175).

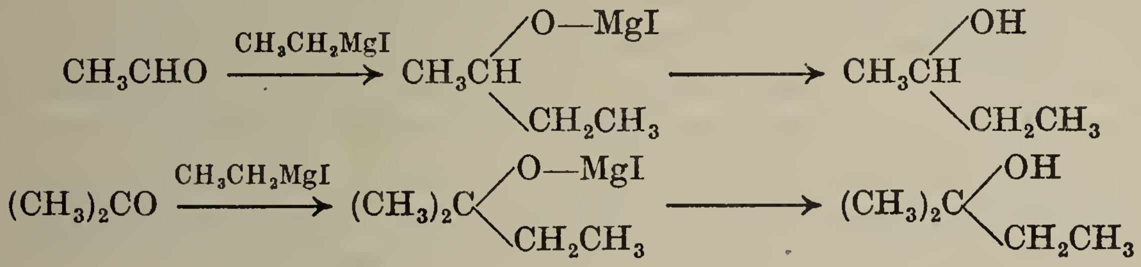
Chlorinated ethers, *e.g.* $ClCH_2 \cdot OCH_3$, and zinc alkyls yield ethers of primary alcohols (Ber. **24**, R. 858) :

$$2Cl \cdot CH_2 \cdot OCH_3 + Zn(C_2H_5)_2 = 2C_2H_5 \cdot CH_2 \cdot OCH_3 + ZnCl_2.$$

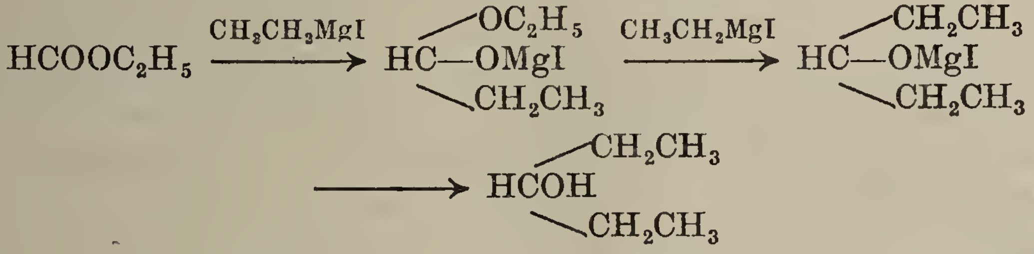
(7) Alkyl magnesium halides react similarly to the zinc alkyls with aldehydes and ketones. They are soluble in ether, are more convenient to deal with and are generally more valuable. The alkyl magnesium halides unite with aldehydes and ketones by breaking the double oxygen bond, and subsequently yield the alcohol on the addition of acidified water to the addition compound. Polymerized formaldehyde (trioxymethylene) gives rise to a primary alcohol, the other aldehydes to secondary and the ketones to tertiary alcohols (Grignard) :

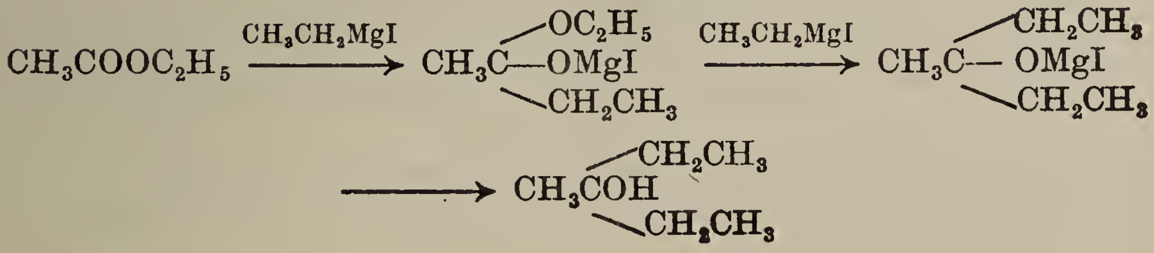
$$H \cdot CHO \xrightarrow{R \cdot MgBr} R \cdot CH_2 \cdot O \cdot MgBr \longrightarrow R \cdot CH_2OH$$

The reaction with trioxymethylene is most conveniently carried out by leading the vapours from boiling, dried trioxymethylene into the well-stirred Grignard reagent (*Ziegler*, Ber. **54**, 737).



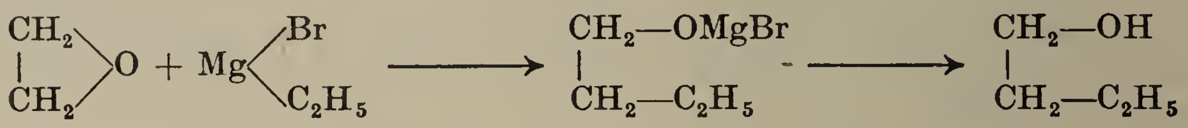
By similar reactions formic acid esters yield secondary alcohols, whilst alkyl carboxylic acid esters and carboxylic acid chlorides and anhydrides give rise to tertiary alcohols :





By the use of the higher alkyl magnesium compounds, secondary alcohols are formed as well as the tertiary, a reduction process taking place (Compt. rend. **141**, 298 : **146**, 343). In many reactions the tertiary alcohols which are first formed, lose water and yield unsaturated hydrocarbons, which may even constitute the main product of the reaction (C. 1901, I. 725 ; II. 622 : 1902, I. 414). Reduction may also occur as a side reaction (Ann. **437**, 256).

Primary alcohols are also obtained by warming the addition-products of ethylene oxide with the alkyl magnesium halides (C. 1903, II. 105 : 1907, I. 1102) :



Tertiary alcohols are also formed by the action of alkyl magnesium compounds on chloroformic esters (Ber. **36**, 3087 : C. 1911, I. 1500).

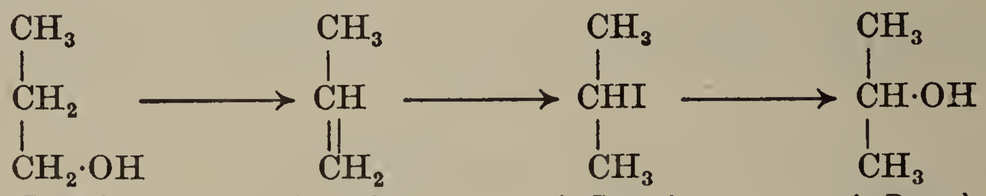
(8) The action of sodium or barium alcoholates on alcohols of the same name—especially among those of high molecular weight—leads to the formation of monohydric alcohols possessing two or three times the carbon content in the molecule (Ber. **34**, 3246 : C. 1902, I. 743). For instance : *iso*amyl alcohol gives rise to a decyl alcohol of the constitution $CHMe_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH(CHMe_2){\cdot}CH_2OH$ (Ann. **318**, 157).

A similar condensation takes place when the vapours of alcohols are passed over heated magnesium, the magnesium alkoxide being produced as an intermediate compound, and then reacting with excess of the alcohol to form the higher alcohol, *e.g.* Propyl alcohol gives β-methylpentanol in 30 per cent. yield (*Terentiev*, Bull. Soc. chim., [iv] **35**, 1145).

In addition to the above universal methods, alcohols are formed by various other reactions. Their formation in the alcoholic fermentation of sugars in the presence of ferments is of great practical importance. Appreciable quantities of methyl alcohol are produced in the dry distillation of wood. Many alcohols, too, exist in combination as already formed natural products in compounds, chiefly as compound esters of organic acids.

Their formation by the breakdown of α- amino acids by yeast fermentation and the action of other micro-organisms is of biological interest (see formation of Fusel Oil, p. 141).

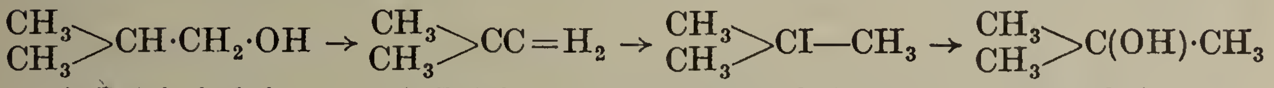
Conversion of Primary into Secondary and Tertiary Alcohols.—By the elimination of water the primary alcohols become unsaturated hydrocarbons C_nH_{2n} (p. 104). The latter, treated with concentrated HI, yield iodides of secondary alcoholic radicals, as iodine does not attach itself to the terminal but to the less hydrogenized carbon atom (p. 106). Secondary alcohols result when these iodides are acted on with silver oxide. The successive conversion is illustrated in the following formulæ :



$$\begin{matrix} CH_3 \\ | \\ CH_2 \\ | \\ CH_2{\cdot}OH \end{matrix} \longrightarrow \begin{matrix} CH_3 \\ | \\ CH \\ \| \\ CH_2 \end{matrix} \longrightarrow \begin{matrix} CH_3 \\ | \\ CHI \\ | \\ CH_3 \end{matrix} \longrightarrow \begin{matrix} CH_3 \\ | \\ CH{\cdot}OH \\ | \\ CH_3 \end{matrix}$$

Propyl alcohol. Propylene. *iso*Propyl iodide. *iso*Propyl alcohol.

In a similar manner primary alcohols in which the group $CH_2\cdot OH$ is joined to a secondary radical, pass into tertiary alcohols :



$$\begin{matrix}CH_3\\CH_3\end{matrix}\!>CH\cdot CH_2\cdot OH \rightarrow \begin{matrix}CH_3\\CH_3\end{matrix}\!>CC=H_2 \rightarrow \begin{matrix}CH_3\\CH_3\end{matrix}\!>CI-CH_3 \rightarrow \begin{matrix}CH_3\\CH_3\end{matrix}\!>C(OH)\cdot CH_3$$

*iso*Butyl alcohol. *iso*Butylene. Tertiary butyl iodide. Tertiary butyl alcohol.

The change is better effected by the aid of sulphuric acid. The sulphuric esters (p. 167), arising from the alkylenes, C_nH_{2n}, have the sulphuric acid residue linked to the carbon atom with the least number of attached hydrogen atoms.

Physical Properties.—In physical properties alcohols exhibit a gradation corresponding with their increase in molecular weight like other bodies belonging to homologous series. The lower alcohols are mobile liquids, dissolving readily in water, and possessing the characteristic alcoholic odour and burning taste. As their carbon content increases, their solubility in water grows rapidly less. The normal alcohols, containing from one to sixteen carbon atoms, are liquid at the ordinary temperature, whilst the higher members are crystalline solids, without odour or taste, resembling the fats. The boiling points of alcohols of similar structure increase gradually in proportion to the increase of their molecular weights, the rise being about 20° for a difference of CH_2. The primary alcohols boil higher than the isomeric secondary, and the latter higher than the tertiary alcohols. Here we observe again that the boiling points are lowered by an accumulation of methyl groups.

The boiling points can be calculated with approximate accuracy from the alkyl residues present (Ber. **20**, 1948). The higher members are only volatile without decomposition under diminished pressure.

Chemical Properties and Reactions.—The alcohols are neutral compounds. In many respects the first members of the series resemble water, and enter into combination with many salts, in which they behave as alcohol of crystallization (p. 137).

Some of the more important reactions are—

(1) The hydroxyl hydrogen is easily replaced by sodium, potassium, and other metals, yielding thereby the alcoholates or alkoxides (p. 144).

(2) In their interaction with strong acids water separates and esters are produced. This reaction, in which the alcohols figure as the base, is analogous to that taking place in the formation of a salt from a basic hydroxide and an acid, but differs from salt formation in that it is not an " ionic " reaction, and takes place correspondingly slowly.

The *haloid esters* of the alcohols are produced when the alcohols are heated together with the halogen acids. These esters are the mono-halogen derivatives of the paraffins. A more convenient method for their formation consists in heating the alcohols with the phosphorus halides. Nascent hydrogen, acting on these esters, affords a means of reconverting the alcohols into their corresponding hydrocarbons (p. 95).

(3) The primary saturated alcohols, on being passed over finely divided metals (Cu, Ni, Zn, Al) heated to redness, are decomposed

into aldehydes. Similarly, secondary alcohols give rise to ketones, and tertiary alcohols to olefines (C. 1903, I. 1212 : J. pr. Chem. [2] **67**, 420 : C. 1908, I. 1375).

(4) Energetic dehydrating agents convert the alcohols, especially those of the tertiary class, into olefines.

(5) Alcohols combine with aldehydes at room temperature, with evolution of heat and formation of hydroxy ethers : these compounds revert to their components at higher temperatures :

$$CH_3CHO + HOEt \rightleftarrows CH_3{\cdot}CH(OH){\cdot}OEt.$$

(Z. physik. Chem. **77**, 284).

In the presence of hydrochloric acid, the compounds combine to form acetals, $R'{\cdot}CH(OR)_2$.

Reactions distinguishing Primary, Secondary, and Tertiary Alcohols.—(1) In the preliminary description of the alcohols it was clearly shown that primary alcohols, upon oxidation, yield aldehydes and carboxylic acids ; that the secondary alcohols form ketones with the same number of carbon atoms, and that the tertiary alcohols break down.

(2) If the alcohols be converted by phosphorus iodide into their iodides, and the latter are changed by silver nitrite to nitroparaffins, these will show characteristic colour reactions, according as they contain a primary, secondary, or tertiary alcohol radical.

(3) Acetic esters are formed when the primary and secondary alcohols are heated with acetic acid to 155° C. The tertiary alcohols, under similar treatment, lose water and form olefines (Ann. **190**, 343 : **197**, 193 : **220**, 165).

(4) When the primary alcohols are heated with soda-lime they yield their corresponding acids :

$$R{\cdot}CH_2{\cdot}OH + NaOH = R{\cdot}CO{\cdot}ONa + 2H_2.$$

(5) PCl_3 reacts with the primary alcohols to form mainly esters of the type $RO{\cdot}PCl_2$; with secondary alcohols it produces unsaturated hydrocarbons, and with tertiary alcohols the corresponding alkyl chlorides (C. 1897, II. 334).

(6) Primary and secondary alcohols yield the corresponding acetic acid esters with acetyl chloride CH_3COCl ; the tertiary alcohols, on the contrary, give rise to tertiary alkyl halides (C. 1906, II. 747).

A. SATURATED ALCOHOLS, PARAFFIN ALCOHOLS, $C_nH_{2n+1}OH$

The most important members of this series, and of the monohydric alcohols in particular, are *methyl alcohol* or *wood spirit*, $CH_3{\cdot}OH$, and *ethyl alcohol* or *spirits of wine* : $CH_3{\cdot}CH_2{\cdot}OH$.

1. Methyl Alcohol, *Wood Spirit*, *Carbinol* [*Methanol*], $CH_3{\cdot}OH$.

History.—Boyle discovered wood spirit in 1661 among the products of the dry distillation of wood. In 1812 Taylor recognized it as being similar to spirits of wine, but considered it an entirely different body. Dumas and Péligot (1831) (Ann. **15**, 1) made the first study of it.

It is formed in large amounts in the dry distillation of wood. The name methyl is derived from μέθυ (wine), and ὕλη (wood).

The aqueous product obtained in the distillation of wood at 500° in iron retorts contains methyl alcohol, acetone, acetic acid, methyl acetate, and other compounds. It is distilled over quick-lime or soda, whereby the acetic acid is held back in the form of a salt. Further purification is effected by means of anhydrous calcium chloride, which combines with the alcohol to a crystalline compound. This is removed, freed from acetone by filtration and drying, and afterwards decomposed by distilling with water. Pure aqueous methyl alcohol passes over, which is then dehydrated with lime or anhydrous potassium carbonate. To procure it perfectly pure it is necessary to decompose methyl oxalate, a readily crystallizable substance, the high-boiling methyl benzoate, or methyl formate, with potassium hydroxide.

Methyl alcohol is also produced in the dry distillation of molasses. It occurs in nature as methyl salicylate, $C_6H_4(OH)\cdot COOCH_3$, *wintergreen oil*, derived from *Gaultheria procumbens*; as the methyl ester of anthranilic acid in *neroli oil*, in many alkaloids and other compounds.

The full synthesis of methyl alcohol proceeds from carbon disulphide through methane and methyl chloride, by the action of aqueous potassium hydroxide on the latter at 100° (*Berthelot*, 1858, Ann. chim. phys. [3] **52**, 101):

$$CS_2 \longrightarrow CH_4 \longrightarrow CH_3Cl \xrightarrow{KOH} CH_3\cdot OH.$$

In Germany at the present time, methyl alcohol is largely manufactured synthetically by the reduction of carbon monoxide by hydrogen (water-gas) under pressure in the presence of catalysts (*Badische Anilin und Sodifabrik*).

To detect ethyl alcohol in methyl alcohol, the liquid is heated with concentrated sulphuric acid, when ethylene is formed from the ethyl alcohol, whilst methyl ether results from the methyl alcohol. The amount of methyl alcohol in wood spirit is determined, quantitatively, by converting it into methyl iodide, CH_3I, through the agency of PI_3 (Ber. **9**, 1928), or into methyl nitrite by the action of nitrous acid. Methyl nitrite is readily volatile, and when distilled into acid potassium iodide solution, liberates iodine, which can be titrated with thiosulphate (Ber. **57**, 693).

Physical Properties.—Methyl alcohol is a mobile liquid with a spirituous odour and a burning taste. It is miscible with water, other alcohols, ether and many other organic liquids. B.p. 64·56°/760 mm., m.p. $-94°$ (Ber. **33**, 638), D^{15} 0·79647 (Ber. **41**, 4326).

Uses.—Wood spirit is employed as a source of heat, and as a denaturizing agent for ethyl alcohol. It is also used in making varnishes, dimethylaniline, and for the methylation of many carbon derivatives, particularly the dye-stuffs. It is a good solvent for many compounds of carbon.

Chemical Properties.—(1) Methyl alcohol combines directly with $CaCl_2$, to form $CaCl_2\cdot 4CH_4O$, crystallizing in brilliant six-sided plates; homologous alcohols give similar compounds (C. 1906, II. 1715). Barium oxide dissolves in methyl alcohol, forming the crystalline body $BaO\cdot 2CH_4O$. The alcohol in this salt behaves as *alcohol of crystallization.*

(2) Potassium and sodium dissolve in the anhydrous alcohol, to form methylates, *e.g.* CH_3OK and CH_3ONa.

(3) Oxidizing agents, *e.g.* air in presence of platinum black or copper oxide, oxidize methyl alcohol to formaldehyde, formic acid, and carbon dioxide.

(4) Chlorine and bromine do not act so readily on methyl as on ethyl alcohol. Chlorine attacks aqueous methyl alcohol, however,

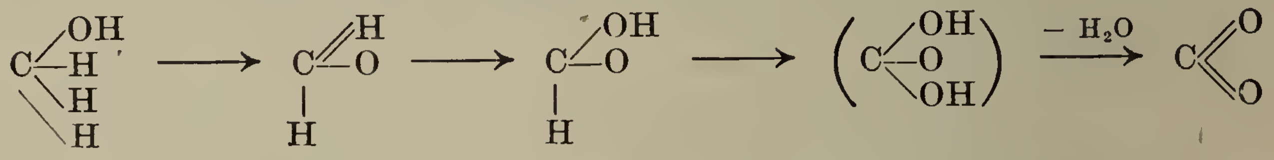
quite easily (Ber. **28**, R. 771). Dichloromethyl ether, $(ClCH_2)_2O$, is first produced, which water converts into formaldehyde and hydrochloric acid (Ber. **26**, 268).

(5) When methyl alcohol is heated with soda-lime, sodium formate results with evolution of hydrogen:

$$CH_2{\cdot}OH + NaOH = CHO{\cdot}ONa + 2H_2.$$

(6) When the alcohol is distilled over zinc dust, it breaks down into carbon monoxide and water.

(7) Methyl alcohol differs from all other primary alcohols in that it contains the CH_2OH group in union with hydrogen. Hence its oxidation is not restricted to the corresponding monobasic carboxylic acid, but may extend to carbonic acid:



2. **Ethyl Alcohol,** *Spirits of Wine* [*Ethanol*], CH_3CH_2OH.—In consequence of its formation in the spirituous fermentation of saccharine plant juices, alcohol, in impure state, was known to the ancients. It was, however, only at the end of the eighteenth century that the knowledge of how it might be obtained in an anhydrous condition was first acquired. In 1808 Saussure determined its constitution.

Occurrence.—Ethyl alcohol seldom occurs in the vegetable kingdom. It is found, together with ethyl butyrate, in the unripe seeds of *Heracleum giganteum* and *Heracleum spondylium*. It is said to be present in the urine of diabetic patients. It appears in that of healthy men after excessive consumption of alcoholic beverages.

Formation.—It may be obtained by the general methods previously described for primary alcohols: (1) From ethyl chloride; (2) from ethyl sulphate; (3) from ethylene chlorhydrin; (4) from ethylamine; (5) from aldehyde; and (6) from acetyl chloride or acetic esters.

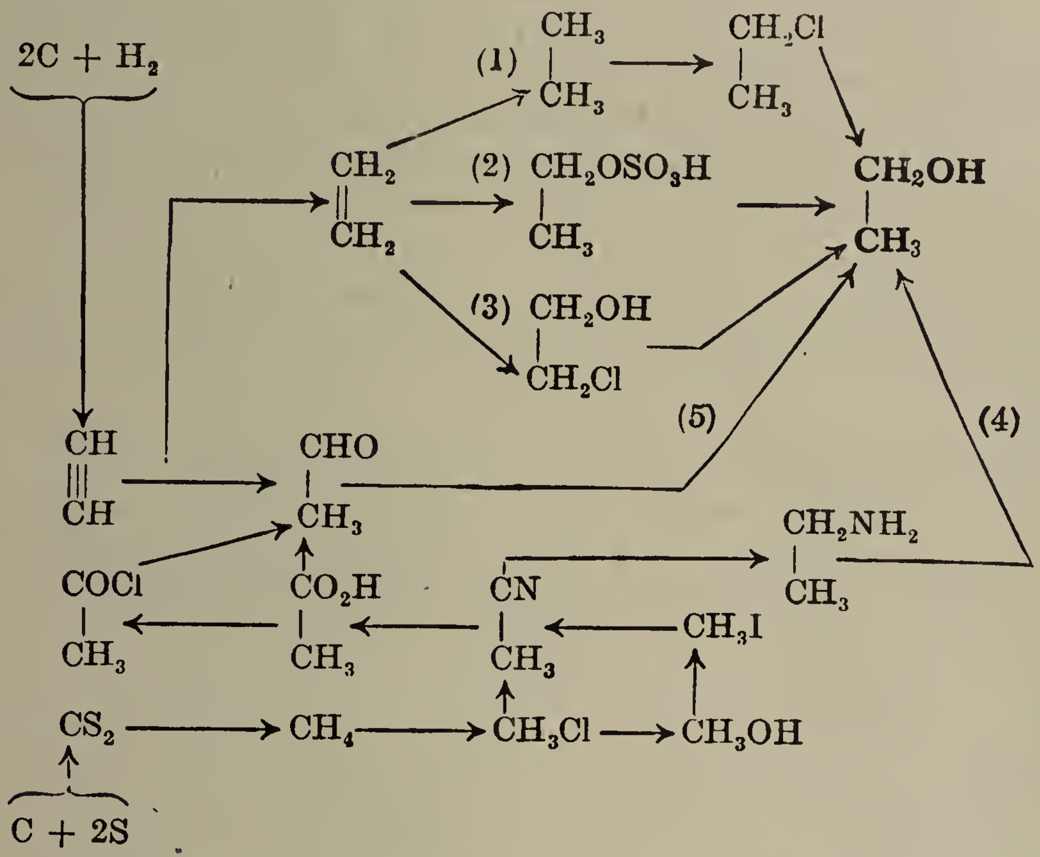
The first three methods show the close relationship between ethyl alcohol, and acetylene, ethylene and ethane, and the last three with methyl alcohol and with acetic acid, whose nitrile can easily be obtained from methyl alcohol.

Starting with acetylene, the most direct course to ethyl alcohol would be through acetaldehyde. Water converts it into the latter (p. 110), and nascent hydrogen then reduces the aldehyde to alcohol.

If the acetylene be changed to ethylene, then various possibilities arise for the formation of ethyl alcohol: (1) Ethylene and hydrogen unite to form ethane, which chlorine changes to ethyl chloride, yielding alcohol when heated with water. (2) At 160° ethylene unites with sulphuric acid, forming ethyl sulphuric acid, which boiling water changes to ethyl alcohol and sulphuric acid. In this manner Berthelot first carried out the synthesis of ethyl alcohol (C. 1899, I. 1018). (3) Ethylene and hypochlorous acid yield ethylene chlorhydrin or monochlorethyl alcohol which may be reduced to ethyl alcohol.

A nucleus-synthesis of ethyl alcohol from methyl alcohol is possible through acetaldehyde. Methyl alcohol can be synthesized from carbon disulphide (p. 137). Phosphorus iodide converts the methyl alcohol into methyl iodide, and this, by action of potassium cyanide, is changed into methyl cyanide. Boiling alkali transforms the latter into an alkali acetate, which phosphorus oxychloride converts into acetyl chloride. The latter, by reduction, yields ethyl alcohol, with acetaldehyde as an intermediate product. Acetaldehyde may also be prepared from calcium acetate by heating it with calcium formate.

These relations are made clear in the following diagram:



Preparation.—Ethyl alcohol is prepared on a technical scale almost exclusively by the alcoholic fermentation of saccharine liquids.

Schwaan, in 1836, and independently *Cagniard Latour*, found that alcoholic fermentation was brought about by yeast cells. This discovery, as opposed to *Liebig's* mechanical fermentation theory (Ann. **29**, 100 : **30**, 250, 363), only found general acceptance from 1857 onwards, through Pasteur's investigations (Ann. chim. phys. [3] **58**, 323). In 1897, *Buchner* showed that the expressed liquid from mechanically broken-up yeast cells could also bring about alcoholic fermentation. It was therefore shown that fermentation was a purely chemical reaction, and not a " vital " process. The active agent in the fermentation is an enzyme-complex *zymase* which is formed by the living yeast cell, but which acts independently of it. Harden and Young in 1906 showed that the enzyme could be split into at least two parts, the zymase itself—heat-labile, non-diffusible—and the " co-enzyme " which is heat-stable and readily diffusible. Both components are simultaneously necessary for alcoholic fermentation. The co-enzyme is probably a hexosephosphate (Ber. **32**, 2086 : **33**, 971, 2764 : **47**, 853 : Bull. [4] **7**, 1 : Proc. Roy. Soc. **77**, [B], 405 : Biochem. Z., **8**, 520). The reaction mechanism of alcoholic fermentation is discussed later. See p. 140.

Conditions of Alcoholic Fermentation.—The yeast germs increase by budding in dilute, warm (5–30°) sugar solutions : the growth is most rapid at 20–30° C. Its development requires salts, especially phosphates, and albuminous substances which are always present in sugar-containing fruit juices as well as oxygen at the commencement (Ber. **29**, 1983), but the fermentation proceeds afterwards without access of air. When the quantity of alcohol in a fermenting liquid reaches a certain amount, the fermentation ceases, since the yeast germs cannot grow in liquids containing 14 per cent. of alcohol. They are also destroyed by a temperature of 60°, and by small quantities of phenol, salicylic acid, mercuric chloride, and other disinfectants.

The sugars occurring in ripening fruits—grapes, apples, cherries—and in cane and beet, as well as in many other plants, belong to the class of carbohydrates, which contain carbon, together with hydrogen and oxygen in the same proportion in which they are present in water. The carbohydrates will be discussed in detail immediately after the hexahydric alcohols: $C_6H_8(OH)_6$—mannitol, dulcitol, sorbitol, etc., of which the first oxidation products are the simple carbohydrates, $C_6H_{12}O_6$.

The carbohydrates may be arranged in three principal classes:

(1) *Monosaccharides.* $C_6H_{12}O_6$: glucose, fructose, etc.

(2) *Disaccharides.* $C_{12}H_{22}O_{11}$: maltose, sucrose, lactose, etc.

(3) *Polysaccharides.* $(C_6H_{10}O_5)_n$: starch, glycogen, dextrin, etc.

The carbohydrates of the second and third classes are anhydrides of the monosaccharides.

Some of the monosaccharides, especially glucose and fructose, are capable of direct alcoholic fermentation. Certain disaccharides such as maltose are also directly fermentable, and the other disaccharides and polysaccharides, which are not directly fermentable, can be hydrolysed to the simple fermentable sugars.

Enzymes.—(See also p. 755.) The breakdown of the di- and polysaccharides to mono-saccharides, with the addition of water (*hydrolysis*), can be brought about by enzymes. For alcoholic fermentation the enzymes *invertase* (*saccharase*), *diastase* (*amylase*), and the complex of *zymase* are of importance. The invertase breaks down sucrose into glucose and fructose, amylase breaks down polysaccharides into di- and mono-saccharides and the zymase breaks down the monosaccharides.

According to Pasteur, in the fermentation of monosaccharides, 90–95 per cent. of the sugar breaks down into carbon dioxide and alcohol, according to the equation first put forward by Gay-Lussac (1815):

$$C_6H_{12}O_6 \longrightarrow 2C_2H_6O + 2CO_2.$$

At the same time, glycerol (2–5 per cent.), fusel oil, and some succinic acid are formed, the last especially towards the end of the fermentation (Ber. **27**, R. 671). In fusel oil occur *n*-propyl alcohol, *iso*butyl alcohol, and most important, " fermentation amyl alcohol," which is a mixture of (inactive) *iso*butylcarbinol and optically active *sec.*-butylcarbinol.

Mechanism of Alcoholic Fermentation.—(*Cf. K. Neuberg*, Ber. **55**, 3624: *Harden*, Alcoholic Fermentation, London, 1932.) The mechanism of alcoholic fermentation has been made clear largely by the work of Neuberg, Wohl, v. Euler, Harden and others.

According to Neuberg, the first stage in the reaction is the breakdown of the sugar molecule into two molecules of methylglyoxal (equation I). Although this decomposition has been confirmed by purely chemical means (action of alkalis), and by the action of enzymes (Biochem. Z. **55**, 495: **71**, 144), the details of the breakdown of the C_6 chain and the wandering of the oxygen atoms is not yet clear. There is much evidence that hexosephosphoric esters play an important part (Z. physiol. Chem. **139**, 15: **143**, 77).

Fermentation by yeast juice or dried yeast is markedly increased by the addition of inorganic phosphate to the fermenting liquid. The additional fermentation is associated with the esterification of an equivalent amount of the phosphoric acid, according to the equation (Harden and Young):

$$2C_6H_{12}O_6 + 2PO_4HR_2 = 2CO_2 + 2C_2H_6O + 2H_2O + C_6H_{10}O_4(PO_4R_2)_2$$

which represents the formation of a hexosediphosphoric ester which can actually be isolated. A hexosemonophosphate is formed simultaneously and its formation can be represented by a similar equation.

This effect does not occur with living yeast, but is not therefore of negligible importance. One possible explanation of the difference is that living yeast contains sufficient of the enzyme hexosephosphatase to break down the organic phosphates and ensure an optimum quantity of free phosphate throughout the reaction. For further discussion on this subject, see Harden's book (above).

The next stage of the reaction has also been much investigated. In 1910 it was discovered that pyruvic acid could be smoothly fermented and it was suggested that this acid was an intermediate product (*cf.* Z. angew. Chem. **39**, 951) and that it was formed by a Cannizzaro reaction, two molecules of methylglyoxal yielding one molecule of pyruvic acid and one of glycerol (equation II). Through the action of yet another part of the enzyme complex, a " carboxylase," the pyruvic acid is immediately broken down to acetaldehyde and carbon dioxide (III). A further Cannizzaro reaction between the acetaldehyde and methylglyoxal (IV) gives ethyl alcohol and a further molecule of pyruvic acid, the latter then reacting again according to equation III.

I. $C_6H_{12}O_6 \longrightarrow 2CH_3{\cdot}CO{\cdot}CHO + 2H_2O.$
II. $2CH_3{\cdot}CO{\cdot}CHO + 2H_2O \longrightarrow CH_2OH{\cdot}CHOH{\cdot}CH_2OH + CH_3{\cdot}CO{\cdot}COOH.$
III. $CH_3{\cdot}CO{\cdot}COOH \longrightarrow CH_3{\cdot}CHO + CO_2.$
IV. $CH_3{\cdot}CHO + CH_3{\cdot}CO{\cdot}CHO \longrightarrow CH_3{\cdot}CH_2OH + CH_3{\cdot}CO{\cdot}COOH.$

An important support to this conception of the reaction is given by the results of changing the conditions of reaction. By the addition of sodium sulphite to the fermenting liquid, the acetaldehyde is converted into the addition compound with $NaHSO_3$ as quickly as it is formed, and stage IV of the reaction is completely inhibited. Under these conditions, the enzyme acts according to equation II and the yield of glycerol is greatly increased (Constein und Lüdecke, Ber. **52**, 1385). By the addition of alkalis, the reaction is changed in another way, and there are formed glycerol, carbon dioxide, alcohol and acetic acid, the last two being formed by a " dismutation " of two molecules of acetaldehyde.

The formation of fusel oil and succinic acid has been explained by the work of F. Ehrlich (Ber. **39**, 2301: **43**, 1027: C. 1905, II. 156: 1909, II. 731). These compounds are not produced by the breakdown of the sugar, but by the decomposition of amino acids which always occur in plant-juices and yield the nitrogen necessary for the growth of the yeast cells. The decomposition of the amino acid proceeds through the corresponding α-ketonic acid, and finally yields an alcohol containing one carbon atom less than the original amino acid. The components of fusel oil and their parent amino acids are shown below.

$CH_3{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CO_2H \longrightarrow CH_3{\cdot}CH_2{\cdot}CH_2OH$

α-Aminobutyric acid. — *n*-Propyl alcohol.

$(CH_3)_2{\cdot}CH{\cdot}CH(NH_2){\cdot}CO_2H \longrightarrow (CH_3)_2CH{\cdot}CH_2OH$

Valine. — *iso*Butyl alcohol.

$(CH_3)_2{\cdot}CH{\cdot}CH_2{\cdot}CH(NH_2)CO_2H \longrightarrow (CH_3)_2CH{\cdot}CH_2{\cdot}CH_2OH$

Leucine. — *iso*Butylcarbinol.

$CH_3{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH(NH_2){\cdot}CO_2H \longrightarrow CH_3{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2OH$

*iso*Leucine. — *sec.*-Butylcarbinol.

$CO_2H{\cdot}CH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CO_2H \longrightarrow CO_2H{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$

Glutaminic acid. — Succinic acid.

Alcoholic Beverages.—The materials used in the preparation of alcoholic liquids by means of fermentation are:

1. *Saccharine plant juices.*
2. *Starch-containing substances*, seeds of grain and potatoes. The fermented liquids are directly consumed (wine, beer) or they are first distilled in order to produce the various kinds of spirits, the alcohol content of which may exceed 50 per cent.:

(1) By the fermentation of saccharine juices we obtain:

(*a*) *without subsequent distillation:*
From grapes: wine.
,, apples: cider.
,, currants: currant wine, etc.

(*b*) *with subsequent distillation:*
From wine: cognac.
,, molasses: rum.
,, cherries: "kirschwasser" (Baden).
,, prunes: sliwowitz (Bohemia), etc.

(2) By the fermentation of starch-containing substances, after converting the starch into sugar with malt:

(*a*) *without subsequent distillation:*
Barley: beer.
Wheat: weissbier (Berlin).
Rice: saké (Japan).

(*b*) *with subsequent distillation:*
Barley and rye, wheat or oats, and maize: corn whisky of various kinds.
Rice: arrac (East India).
Potatoes: potato spirit.

Manufacture of Potato Spirit.—Pure ethyl alcohol is obtained from potato spirit. The potatoes are first heated with steam to 140–150° C. under a pressure of from 2 to 3 atmospheres. The lower part of the apparatus is then opened and the potato mash pressed out and digested at 57–60° in a mashing apparatus with finely divided malt mixed with water. In this manner the starch of the potatoes is converted into sugar. When the "mash" has cooled to the proper temperature it is run into the fermentation-tubs, where it comes into contact with "pure culture" of yeast, and is then fermented. Crude spirit results from the distillation of the fermented mash; what remains is known as vinasse.

Manufacture of Pure Absolute Alcohol.—To purify the crude spirit further it is fractionated on a large scale in a column apparatus. The first portions, more readily volatile, contain aldehyde, acetal, and other substances. A purer spirit (containing 95–96 per cent. of alcohol) follows, and in commerce is known as *spirit*. Finally come the "tailings," in which are the fusel oils. To remove the latter, the spirit is diluted with water and passed through previously ignited wood-charcoal, which retains the fusel oils, and the filtrate is then distilled.

To prepare anhydrous alcohol, the rectified spirit (90–95 per cent. alcohol) is distilled with anhydrous potassium carbonate, anhydrous copper sulphate, quick-lime (Ann. **160**, 249), or barium oxide. Commercial absolute alcohol (about 99 per cent.) can be freed from its last traces of aldehyde and water, by treatment with alkali and silver oxide, and subsequent distillation over metallic calcium (Ber. **38**, 3612).

Detection of Water in Alcohol.—Absolute alcohol dissolves barium oxide, assuming a yellow colour at the same time, and does not restore the blue colour to anhydrous copper sulphate. It is soluble without turbidity in a little benzene; when more than three per cent. of water is present, cloudiness ensues. On adding anhydrous or absolute alcohol to a mixture of very little anthraquinone and some sodium amalgam it becomes dark green in colour, but in the presence of traces of water a red coloration appears (Ber. **10**, 927). Aqueous alcohol generates acetylene from calcium carbide, whilst the anhydrous spirit has no action in the cold (C. 1898, I. 658, 1225).

Detection of Alcohol.—Traces of alcohol in solutions are detected and determined either by oxidation to aldehyde (*q.v.*) or by converting it by means of dilute potassium hydroxide and iodine into iodoform (Ber. **13**, 1002).

Its conversion into ethyl benzoate, by shaking with benzoyl chloride and sodium hydroxide (Ber. **19**, 3218; **21**, 2744), also answers for this purpose.

Properties.—Pure alcohol is a colourless mobile liquid with an agreeable ethereal odour. It boils at 78·3°/760 mm., and solidifies when strongly cooled to a varnish-like mass, which melts at − 112°. D^0 0·806, D^{20} 0·789, D^{25} 0·78513. It burns with a non-luminous flame and absorbs water energetically from the air. When mixed with water a contraction occurs, accompanied by rise of temperature; the maximum is reached when one molecule of alcohol is mixed with three molecules of water, corresponding with the formula $C_2H_6O + 3H_2O$. The amount of alcohol in aqueous solutions is given either in per cent. by weight (degrees according to Richter) or per cent. by volume (degrees according to Tralles). It may be determined by an *alcoholometer*, the scale of which gives directly the per cent. by weight or volume for a definite temperature (15° C.). Or the vapour tension is ascertained by means of the *vapourimeter* of Geissler, or the boiling point is determined with the *ebullioscope*.

The alcohol contained in spirituous beverages is first distilled off and then estimated in the distillate.

Alcohol dissolves many mineral salts, the alkalis, hydrocarbons, resins, fatty acids, and almost all the carbon derivatives. The majority of gases are more readily soluble in it than in water; 100 volumes of alcohol dissolve 7 volumes of hydrogen, 25 volumes of oxygen, and 16 volumes of nitrogen.

Ethyl alcohol forms crystalline compounds with some salts, *e.g.* calcium chloride and magnesium chloride, in which it behaves analogously to water of crystallization.

Reactions.—(1) Potassium and sodium dissolve in it, yielding the alcoholates.

(2) With sulphuric acid it yields ethyl hydrogen sulphate, and with sulphuric anhydride, carbyl sulphate (p. 103).

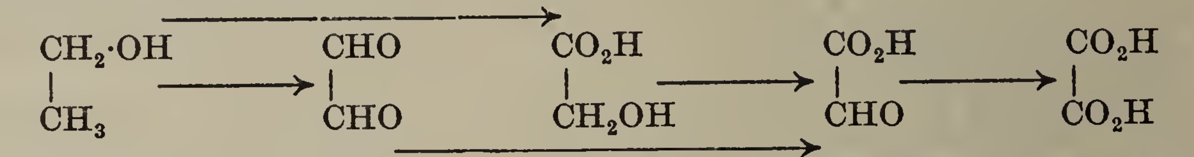
(3) Phosphorus bromide and iodide change it into ethyl bromide and ethyl iodide.

(4) Being a primary alcohol, such oxidants as manganese peroxide and sulphuric acid, chromic acid, platinum black and air, convert it to acetaldehyde and acetic acid (p. 128).

(5) Chlorine and bromine oxidize alcohol to acetaldehyde, which unites with more alcohol to form acetal. The further action of chlorine

leads to the formation of mono- and dichloroacetal, and finally to chloral alcoholate. Bleaching powder changes alcohol to chloroform, and iodine and potassium hydroxide convert it into iodoform.

(6) Nitric acid, free from nitrous acid, changes alcohol into ethyl nitrate (*q.v.*). Under certain conditions alcohol can be so oxidized by nitric acid that, besides attacking the $CH_2·OH$ group, the methyl group may be changed with the resulting formation of glyoxal, glycollic acid, glyoxalic acid, and oxalic acid :



$$\begin{tikzcd} \begin{array}{c}CH_2{\cdot}OH\\ |\\ CH_3\end{array} \arrow[r] & \begin{array}{c}CHO\\ |\\ CHO\end{array} & \begin{array}{c}CO_2H\\ |\\ CH_2OH\end{array} \arrow[r] & \begin{array}{c}CO_2H\\ |\\ CHO\end{array} \arrow[r] & \begin{array}{c}CO_2H\\ |\\ CO_2H\end{array} \end{tikzcd}$$

Ethyl alcohol. Glyoxal. Glycollic acid. Glyoxalic acid. Oxalic acid.

(7) Mercury fulminate (*q.v.*) is produced when alcohol acts on mercury and an excess of nitric acid. Boiling with mercuric oxide and sodium hydroxide gives rise to a basic, explosive body, $C_2Hg_6O_4H_2$, called mercarbide (*cf.* p. 537) (Ber. **33**, 1328).

(8) If alcohol be passed through a red-hot tube, decomposition will be found to begin at 800°, and at 820–830°, about $\frac{1}{5}$ of it splits up into ethylene and water, and $\frac{4}{5}$ into aldehyde and hydrogen, whilst $\frac{2}{3}$ of the aldehyde further breaks down into methane and carbon monoxide (Ber. **34**, 3579). These decomposition products appear at lower temperatures by passing alcohol vapour over finely divided metals or aluminium oxide (C. 1903, I. 955 : II. 335).

Alcoholates.—Sodium ethoxide is the most important alcoholate, as it is employed in a series of nucleus-synthetic reactions. It affords a means of splitting off water and alcohol. It may be prepared by dissolving sodium in alcohol, then heating it to 200° C. in an atmosphere of hydrogen to free it from alcohol, when it forms a white, voluminous powder (Ann. **202**, 294 : Ber. **22**, 1010). Or, a calculated quantity of metallic sodium is added to a solution of alcohol in ether, toluene, or xylene, and the whole is heated under a reflux condenser until the sodium has entirely disappeared (Ber. **24**, 649 : **37**, 2067). An excess of water changes the alcoholates to alcohol and sodium hydroxide ; with a small amount of water the reaction is incomplete. The alcoholates also result on dissolving KOH and NaOH in strong alcohol. Sodium peroxide converts alcohol into sodium alcoholate and sodium hydroperoxide, NaO·OH (Ber. **27**, 2299).

Calcium ethoxide, $Ca(OC_2H_5)_2$, is formed by the solution of metallic calcium in alcohol, or by the decomposition of calcium carbide by absolute alcohol with the aid of heat (Ber. **28**, R. 61 : **38**, 3614).

Aluminium ethoxide, $Al(OC_2H_5)_3$, m.p. 134°, b.p. 205°/14 mm. ; *aluminium propylate* $Al(OC_3H_7)_3$, m.p. 106°, b.p., 24°/14 mm., are remarkable in that they are volatile without decomposition under much reduced pressure. *Aluminium methoxide* is decomposed by heat under reduced pressure. These compounds are prepared by the action of the respective alcohols on amalgamated aluminium (C. 1900, I. 10, 585).

Substituted Ethyl Alcohols :

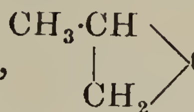
1.	$CH_2Cl{\cdot}CH_2OH$	*Glycol chlorhydrin* (Bromhydrin, Iodohydrin).
2.	$CHCl_2{\cdot}CH_2OH$	*Dichloroethyl alcohol*, b.p. 146° (Ber. **20**, R. 363).
3.	$CCl_3{\cdot}CH_2OH$	*Trichloroethyl alcohol*, m.p. 18°, b.p. 151° (Ann. **210**, 63).
4.	$CHBr_2CH_2OH$	*Dibromoethyl alcohol*, b.p. 70–72°/10 mm. (Ber. **56**, 2283).
5.	CBr_3CH_2OH	*Tribromoethyl alcohol*, m.p. 80°, b.p. 92–94°/10 mm. (Ber. **56**, 2283).
6.	$CH_2NO_2{\cdot}CH_2OH$	*Nitroethyl alcohol*, b.p. 103°/11·5 mm. (Ber. **53**, 209).
7.	$CH_2NH_2{\cdot}CH_2OH$	*Hydroxyethylamine* (β-Aminoethyl alcohol).
8.	$CH_3{\cdot}CH(NH_2)OH$	*Aldehyde-ammonia* (α-Aminoethyl alcohol).

The compounds 1, 6, and 7 will be discussed with ethylene glycol, 8, with acetaldehyde. *Di-* and *trichloroethyl alcohol* are obtained by the action of zinc ethyl on di- and trichloroacetaldehyde. The trichloro-compound is also obtained from urochloralic acid (*q.v.*) and by the biochemical reduction of chloral by yeast (Lintner and Lüers, Z. physiol. Chem. **88**, 122 : Willstätter, Ber. **56**, 2283). *Trichloroethyl carbamate*, $NH_2COOCH_2CCl_3$ *voluntal*, is used as a hypnotic (C. 1923, I. 1196). *Tribromoethyl alcohol* is obtained by the biochemical reduction of tribromoacetaldehyde (bromal) by means of yeast. Dibromoethyl alcohol is formed as a by-product.

3. **Propyl Alcohols** [*Propanols*], $C_3H_7\cdot OH$.—Two isomeric propyl alcohols are theoretically possible: the primary normal propyl alcohol and the secondary *iso*propyl alcohol. Their constitution is evident from their methods of formation and their reactions (pp. 133–134).

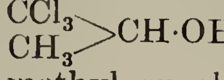
Normal propyl alcohol, $OH_3\cdot OH_2\cdot OH_2\cdot OH$, b.p. 97·4° ; $D_{20} =$ 0·8044, occurs in fusel oil (*Chancel*, 1853) from which it is obtained by fractional distillation. It is an agreeable-smelling liquid, which is miscible in every proportion with water, but is insoluble in a saturated, cold calcium chloride solution, whereby it can be distinguished from ethyl alcohol. It can also be prepared from ethyl magnesium chloride and trioxymethylene (p. 133), and by reduction of propionaldehyde. Oxidation converts it first to propionaldehyde, and finally to propionic acid. By sulphuric acid it is converted into propylene, which with hydriodic acid yields *iso*propyl iodide, which can be converted into *iso*propyl alcohol.

*iso***Propyl alcohol** (*Secondary Propyl alcohol, dimethylcarbinol*), b.p. 82·7°, D^{20} 0·7887, was prepared in 1855 by Berthelot from propylene and sulphuric acid, and in 1862 by Friedel by the reduction of acetone. Kolbe in 1862 (Z. Chem. 1862, 687) recognized in *iso*propyl alcohol the first representative of the class of secondary alcohols predicted by him (p. 128).

It may be obtained from propylene oxide,  $\left.\begin{matrix}CH_3\cdot CH\\ |\\ CH_2\end{matrix}\right>O$, by reduction; from formic ester by the aid of zinc and methyl iodide, and from acetaldehyde by means of methyl magnesium iodide (p. 220). Its formation from normal propylamine by the action of nitrous acid is noteworthy, and is accompanied by the simultaneous production of primary propyl alcohol and propylene.

It is prepared catalytically by the reduction of acetone (Swiss Pat. 87962 : C. 1921, IV. 421).

The most practical method of obtaining it is to boil the iodide, which is easily prepared from glycerol, with ten parts of water and freshly prepared lead hydroxide in a vessel connected with a reflux condenser, or by simply heating the iodide with twenty volumes of water to 100° (Ann. **186**, 391). Oxidation changes it into acetone, whilst chlorine converts it into unsymmetric tetrachloroacetone (*q.v.*).

*Trichloro*iso*propyl alcohol*,  $\left.\begin{matrix}CCl_3\\ CH_3\end{matrix}\right>CH\cdot OH$, m.p. 49°, b.p. about 153°, is produced by the action of zinc methyl on chloral (p. 238) (Ann. **210**, 78).

4. **Butyl Alcohols,** $C_4H_9\cdot OH$.—According to theory four isomerides are possible : 2 primary, 1 secondary, and 1 tertiary (p. 128) :

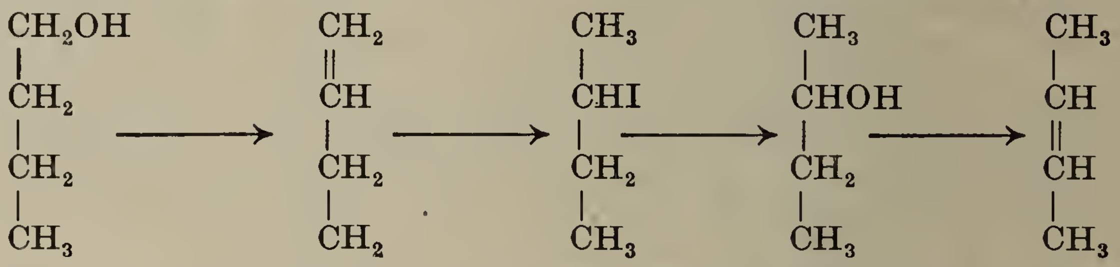
Name.	Formula.	M.P.	B.P.	Sp. Gr.
1. Normal Butyl Alcohol	$CH_3(CH_2)_2CH_2OH$	Liquid	116·8°	0·8099 at 20°
2. *iso*Butyl Alcohol . .	$(CH_3)_2\cdot CH\cdot CH_2OH$	,,	108·4°	0·8020 at 20°
3. Secondary Butyl Alcohol	$\begin{matrix}CH_3\cdot CH_2\\ CH_3\end{matrix}\!\!>\!CH\cdot OH$	,,	99°	0·8270 at 0°
4. Tertiary Butyl Alcohol	$(CH_3)_3C\cdot OH$	25°	83°	0·7788 at 30°

Normal butyl alcohol, n-*Propylcarbinol* [1-*Butanol*], is formed in the action of sodium amalgam on normal butyl aldehyde (Method 4*a*, p. 131), and from ethylene oxide and ethyl magnesium bromide (Method 7, p. 134). It is further produced by the fermentation of glycerol by a micro-organism together with trimethylene glycol, $CH_2OH\cdot CH_2CH_2OH$ (*Fitz*, Ber. **16**, 1438 : **29**, R. 72 : *Buchner* and *Meisenheimer*, Ber. **41**, 1410).

Trichlorobutyl alcohol, $CH_3\cdot CHCl\cdot CCl_2\cdot CH_2\cdot OH$, m.p. 62°, b.p. 120°/45 mm., results when zinc ethyl and butyl chloral (p. 240) are brought together, and is also obtained from urobutylchloralic acid (Ann. **213**, 372).

Secondary butyl alcohol, *Methylethylcarbinol*, *Butylene hydrate*, [2-*Butanol*], is a strongly-smelling liquid. It is obtained from methyl ethyl ketone by reduction with sodium and water under ether (C. 1901, II. 1113) ; also from normal butyl alcohol by conversion into butylene, by loss of water, the addition of hydrogen iodide to the butylene, and finally the hydrolysis of the iodide produced (p. 134). The same iodide is formed on heating erythritol, $CH_2OH[CHOH]_2CH_2OH$, with hydriodic acid. Heated to 140–250°, it decomposes into water and β-butylene, $CH_3\cdot CH : CH\cdot CH_3$.

The relations existing between the normal primary and secondary butyl alcohols, as well as between α-butylene and β-butylene, are shown in the following arrangement :



$$\begin{matrix}CH_2OH\\ |\\ CH_2\\ |\\ CH_2\\ |\\ CH_3\end{matrix}\longrightarrow\begin{matrix}CH_2\\ \|\\ CH\\ |\\ CH_2\\ |\\ CH_3\end{matrix}\longrightarrow\begin{matrix}CH_3\\ |\\ CHI\\ |\\ CH_2\\ |\\ CH_3\end{matrix}\longrightarrow\begin{matrix}CH_3\\ |\\ CHOH\\ |\\ CH_2\\ |\\ CH_3\end{matrix}\longrightarrow\begin{matrix}CH_3\\ |\\ CH\\ \|\\ CH\\ |\\ CH_3\end{matrix}$$

Secondary butyl alcohol is the simplest *racemic* alcohol (comp. p. 70). It is resolved into its *optically active components* by means of the brucine salt of its acid sulphuric ester, or better by means of its acid phthalate (Ber. **40**, 695 : J.C.S., **103**, 1938).

*iso***Butyl alcohol,** iso*Propylcarbinol*, *Butyl alcohol of fermentation* [2-*Methylpropane*-1-*ol*], occurs in fusel oils and especially in the spirit from potatoes. It is a liquid possessing a characteristic odour. It may readily be changed to *iso*butylene $(CH_3)_2C{=}CH_2$, from which, by the addition of halogen acids, derivatives of tertiary butyl alcohol are obtained (p.135). For the action of chlorine on *iso*butyl alcohol, see Ber. **27**, R. 507 : **29**, R. 922.

Tertiary butyl alcohol, *Trimethylcarbinol*, [*Dimethyl-ethanol*], was prepared by *Butlerow* (Ann. **144**, 1) in 1863, from acetyl chloride and zinc methyl, and was the first representative of the tertiary alcohols predicted by Kolbe.

The oxidation of tertiary butyl alcohol produces *iso*butyric acid $(CH_3)_2\cdot CH\cdot CO_2H$ corresponding with *iso*butyl alcohol. This behaviour may be explained by the intermediate formation of *iso*butylene $(CH_3)_2C{=}CH_2$, the conversion of this, by absorption of water, into *iso*butyl alcohol, and the oxidation of the latter (Ann. **189**, 73). The *iso*butylene, resulting from *iso*butyl alcohol and tertiary butyl alcohol, by the withdrawal of water can, by the addition of HClO and reduction of the resulting chlorhydrin, be changed to *iso*butyl alcohol, and by addition of HI yields tertiary butyl iodide, which in turn may be transformed into the tertiary alcohol (p. 135).

5. **Amyl Alcohols,** $C_5H_{11}\cdot OH$.—Theoretically, 8 isomers are possible : 4 primary alcohols, 3 secondary, and 1 tertiary, all of which are known.

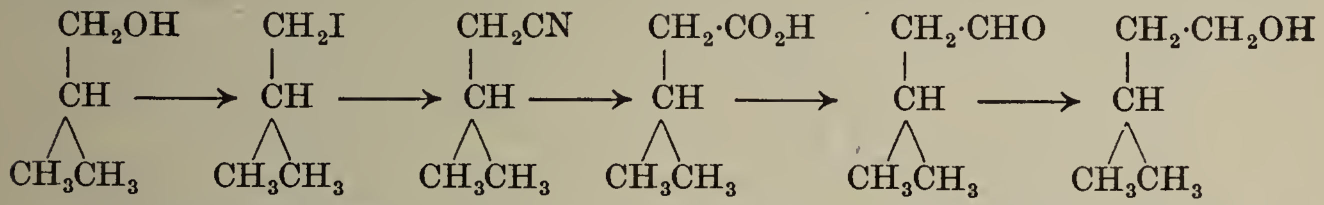
The following table contains the formulæ and the boiling points of the eight amyl alcohols. The name amyl alcohol is derived from ἄμυλον = starch, because the first-discovered amyl alcohol was observed in the fusel oil obtained from potato spirit.

Name.	Formula.	M.P.	$B.P._{760}$
1. Normal Amyl Alcohol . . .	$CH_3\cdot[CH_2]_3CH_2\cdot OH$		137°
2. *iso*Butylcarbinol	$(CH_3)_2\cdot CHCH_2\cdot CH_2OH$		131°
3. Active Amyl Alcohol	$\begin{matrix}CH_3\\CH_3\cdot CH_2\end{matrix}\!>\!\overset{*}{C}H\cdot CH_2OH$		128°
4. *Tert.*-Butylcarbinol	$(CH_3)_3C\cdot CH_2OH$	+ 49°	112°
5. Diethylcarbinol	$(CH_3CH_2)_2CH\cdot OH$		116°
6. Methyl-*n*-propylcarbinol . . .	$\begin{matrix}CH_3\\CH_3\cdot CH_2\cdot CH_2\end{matrix}\!>\!\overset{*}{C}H\cdot OH$		118°
7. Methyl*iso*propylcarbinol . . .	$\begin{matrix}CH_3\\(CH_3)_2\cdot CH\end{matrix}\!>\!\overset{*}{C}H\cdot OH$		112°
8. Dimethylethylcarbinol . . .	$\begin{matrix}(CH_3)_2\\CH_3\cdot CH_2\end{matrix}\!>\!C\cdot OH$	− 12°	102·5°

Three of these eight alcohols contain an asymmetric carbon atom, indicated in the formulæ by a star, hence each can have three modifications, two optically active and one optically inactive (p. 39), which raises the possible number of amyl alcohols to fourteen. On the connection between boiling point and velocity of reaction, see Ber. **30**, 2784.

(1) **Normal amyl alcohol** is most easily prepared from normal amylamine which, in turn, is obtained from caproic acid. It is almost insoluble in water, and has an odour of fusel oil.

(2) ***iso*Butylcarbinol,** $(CH_3)_2CH\cdot CH_2\cdot CH_2OH$, constitutes the chief ingredient of the amyl alcohol of fermentation obtained from fusel oil (p. 142), and occurs as esters of angelic and crotonic acids in Roman camomile oil. It may be obtained in a pure condition by synthesis from *iso*butyl alcohol, with which it occurs in fusel oil :



A simpler synthesis is that from *iso*butyl magnesium bromide and trioxymethylene (Method 7, p. 133) (C. 1904, II. 1599). The so-called *amyl alcohol of fermentation*, b.p. 129–132°, occurs in fusel oil and consists mainly of inactive *iso*butylcarbinol. It possesses a disagreeable odour. In addition, *sec.*-butylcarbinol is present and causes the mixture to be lævo-rotatory.

The different solubilities and crystalline forms of the barium salts of the hydrogen sulphates of the two alcohols distinguish them and assist in their separation. From the more sparingly soluble salt, which forms in rather large quantity, *iso*butylcarbinol may be obtained (*Pasteur*). A more complete separation of the alcohols is reached by conducting HCl into the mixture ; *iso*butylcarbinol will be esterified first, the active amyl alcohol remaining unchanged (Le Bel) (Ann. **220**, 149). A more suitable substance for separating the fermentation amyl alcohols by the esterification method is nitrophthalic acid (Vol. II) (*Markwald*, Ber. **34**, 479 ; **37**, 1038). When the crude fermentation alcohol is distilled with zinc chloride, ordinary amylene is the product ; this consists mainly of $(CH_3)_2C:CH\cdot CH_3$, resulting from a transposition of *iso*butyl carbinol ; it contains, further, γ-amylene and α-amylene (p. 107).

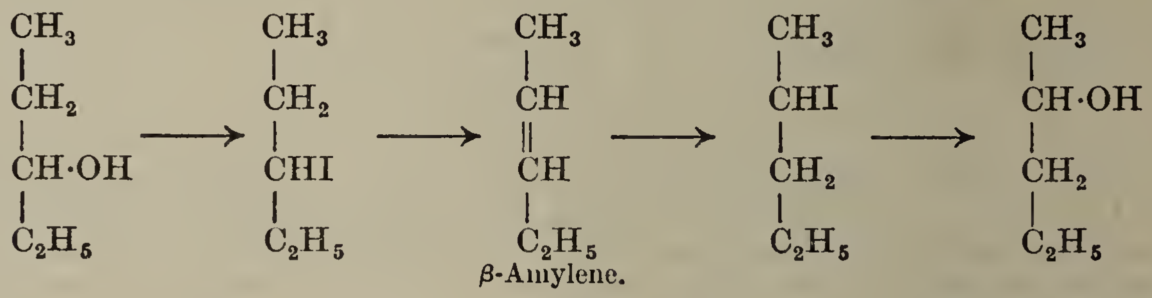
(3) **Active amyl alcohol,** $\begin{matrix}CH_3\\CH_3CH_2\end{matrix}\!>\!\overset{*}{C}H\cdot CH_2OH$, sec.-*Butylcarbinol.* Of

the two active modifications, the lævo-rotatory form, not yet obtained pure, is the optically active constituent of the fermentation alcohol. The proportion of the optically active alcohol in fermentation amyl alcohol varies from 13 to 58 per cent., according to the origin of the latter (Ber. **35**, 1596). Its rotatory power is $[\alpha]_D = -5{\cdot}9°$. The chloride, bromide, iodide, carbamic acid ester, and methylethylacetic acid (see valeric acid) prepared from the lævo-carbinol, are all optically active and dextro-rotatory, whilst the corresponding amine (p. **197**) is lævo-rotatory (Ber. **28**, R. 410; **29**, 59).

The inactive modification of secondary butyl carbinol can be obtained by heating with sodium hydroxide (Le Bel), and also synthetically from secondary butyl magnesium bromide and trioxymethylene (p. 133; C. 1906, I. 130). Resolution by means of a *mucor* leaves the dextro-rotatory alcohol (Ber. **15**, 1506).

(4) *Tert.*-**Butylcarbinol,** $(CH_3)_3{\cdot}C{\cdot}CH_2OH$, is formed on reducing the chloride of trimethylacetic acid or pivalic acid (Ber. **24**, R. 557) with sodium amalgam. Nitrous acid converts its amine, with isomeric change, into dimethylethylcarbinol (Ber. **24**, 2161).

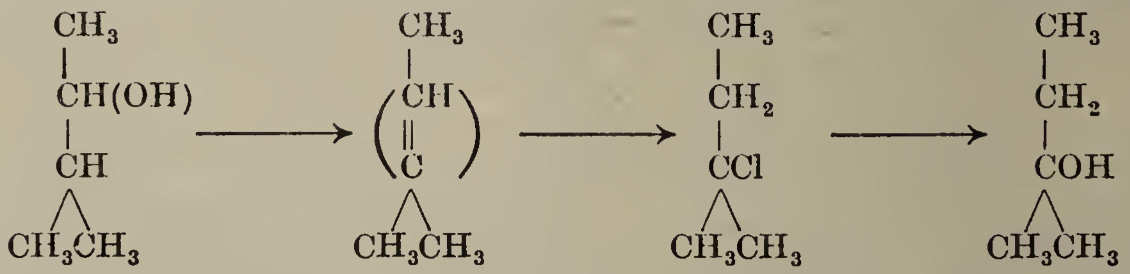
(5) **Diethylcarbinol,** $(C_2H_5)_2{\cdot}CHOH$, is formed by the action of zinc and ethyl iodide upon ethyl formate. Since β-amylene, $C_2H_5{\cdot}CH : CH{\cdot}CH_3$, yields the iodide of methylpropylcarbinol with HI, from which methylpropylcarbinol is obtained, the diethylcarbinol can thus be converted into the latter alcohol :



The two methylpropylcarbinols are obtained from methyl propyl ketone and methyl *iso*propyl ketone by reduction with sodium amalgam.

(6) **Methyl-*n*-propylcarbinol,** $CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{*}{C}H(OH){\cdot}CH_3$, is resolved by *Penicillium glaucum* (Le Bel); the dextro-rotatory modification is destroyed, and the lævo-rotatory form remains.

(7) **Methyl*iso*propylcarbinol,** $(CH_3)_2{\cdot}CH{\cdot}CH(OH){\cdot}CH_3$, yields the derivatives of tertiary amyl alcohol, apparently with the intermediate formation of amylene, $(CH_3)_2C{=}CHCH_3$, when acted on by halogen acids and also PCl_5 :



The true derivatives of methyl*iso*propylcarbinol are obtained from α-*iso*amylene $(CH_3)_2{\cdot}CH{\cdot}CH : CH_2$ (p. 107), by the addition of halogen acids, at ordinary temperatures or when warmed.

(8) **Tertiary amyl alcohol,** $\begin{matrix}(CH_3)_2\\C_2H_5\end{matrix}\!\!>C{\cdot}OH$, *Dimethylethylcarbinol, Amylene hydrate,* is a liquid with an odour like that of camphor. It produces sleep, the same as does chloral hydrate, and is, therefore, produced technically.

Amyl alcohol of fermentation is employed as the parent substance, which, with zinc chloride, yields ordinary amylene, consisting mainly of β-*iso*amylene, $CH_3CH{=}C\!<\!\begin{matrix}CH_3\\CH_3\end{matrix}$ (p. 107). This is shaken at − 20° with sulphuric acid diluted with ½–1 volume of water, and the solution is boiled with water (Ann. **190**, **345**).

It is further formed by the action of nitrous acid on the amine of tertiary butyl carbinol (Ber. **24**, 2519), and from propionyl chloride and zinc methyl. At 200° it decomposes into water and β-*iso*amylene.

Higher Saturated Alcohols, $C_nH_{2n+1}\cdot OH$

Many representatives of the higher members of this series are known. Fourteen of the theoretically possible seventeen hexyl alcohols, and thirteen out of the thirty-eight possible heptyl alcohols are known. Of the higher members, the number theoretically possible rapidly increases, but the known representatives become fewer in number. Few only are of importance, either from their formation, structure, or natural occurrence.

Some of the more important members are described below.

A large number of secondary alcohols of the general formula R·CHOH·R′ have been resolved by means of the brucine, strychnine or cinchonidine salts of their acid phthalates (J.C.S. **99**, 45 : **103**, 1923).

Hexyl alcohol, n-*Hexyl alcohol*, b.p. 157°, occurs as acetic and butyric esters in the oil of the seed of *Heracleum giganteum* (Ann. **163**, 193).

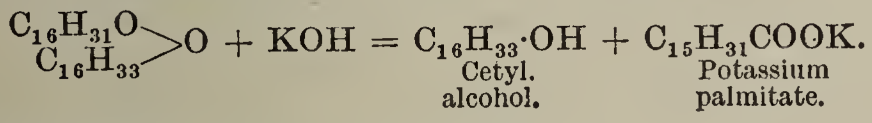
Pinacolyl alcohol $(CH_3)_3C\cdot CHOH\cdot CH_3$, m.p. + 4°, b.p. 120°, results from the reduction of pinacolin (*q.v.*) or *tert.*-butyl methyl ketone, $(CH_3)_3\cdot C\cdot CO\cdot CH_3$. It has a camphor-like odour. (See Ber. **26**, R. 14 ; C. 1901, II. 1157 ; comp. Tetramethylethylene.) The isomeric *βγ-dimethylbutane-β-ol*, m.p. — 10·5°, b.p. 119°, is prepared from acetone and *iso*propyl magnesium bromide. It decomposes when heated with dilute sulphuric acid into H_2O and tetramethylethylene (C. 1906, II. 1718).

n-**Heptyl alcohol,** b.p. 175°, has been prepared from œnanthal (*q.v.*) by reduction, and from *n*-heptane (Ann. **161**, 278). *Pentamethylethyl alcohol*, m.p. + 17°, b.p. 131°, has been obtained by various syntheses by means of magnesium-organic compounds (C. 1906, II. 1718).

n-**Octyl alcohol,** $C_8H_{17}OH$, b.p. 199°, occurs as acetic ester in the volatile oil of *Heracleum spondylium,* as butyric ester in the oil of *Pastinaca sativa,* and in the oil of *Heracleum giganteum* (Ann. **185**, 26). It has been obtained artificially by several methods, amongst others by the reduction of caprylic ester by sodium and alcohol.

n-**Nonyl alcohol** occurs as caprylic ester in orange-flower oil (J. pr. Chem. [2] **62**, 532).

Hexadecyl alcohol, Cetyl alcohol, *Ethal,* $C_{16}H_{33}\cdot OH$, m.p. 49·5°, b.p. 340°, is a white, crystalline mass. It was prepared in 1818 by Chevreul from the cetyl ester of palmitic acid, the chief ingredient of *spermaceti* (see Palmitic acid), by saponification with alcoholic potassium hydroxide :



$$\left.\begin{matrix}C_{16}H_{31}O\\C_{16}H_{33}\end{matrix}\right>O + KOH = \underset{\text{Cetyl. alcohol.}}{C_{16}H_{33}\cdot OH} + \underset{\text{Potassium palmitate.}}{C_{15}H_{31}COOK}.$$

(*Preparation*, see J. Ind. Eng. Chem. **9**, 1123).

When fused with potassium hydroxide, it yields palmitic acid (p. 306) :

$$C_{15}H_{31}CH_2OH + KOH = C_{15}H_{31}COOK + 2H_2.$$

Eicosyl alcohol, $C_{20}H_{41}\cdot OH$, m.p. 40° (J.C.S. **127**, 70).

Ceryl alcohol, $C_{26}H_{53}OH$ (or $C_{27}H_{55}OH$, Compt. rend. **170**, 1326) m.p. 80°. The cerotate forms *Chinese Wax,* which is a waxy mass formed on the Chinese Ash, *Fraxinus Chinensis,* by an insect *Corcus coniferus* and the alcohol is obtained from the ester by fusion with potassium hydroxide.

Melissyl alcohol, *Myricyl alcohol,* $C_{30}H_{61}\cdot OH$, m.p. 85°, occurs as myricyl palmitate in beeswax, from which it is isolated in the same manner as the preceding compound. *Chloride,* m.p. 64° ; *iodide,* m.p. 69·5°. Myricyl iodide and metallic sodium give *hexacontane,* $C_{60}H_{122}$, or *dimyricyl* (Compt. rend. **170**, 886).

Montanyl alcohol, $C_{28}H_{57}OH$, m.p. 83·5°, **Gossypyl alcohol,** $C_{30}H_{61}OH$, m.p. 85°, and two *alcohols,* $C_{32}H_{65}OH$ and $C_{34}H_{69}OH$, m.pp. 87–87·5° and 88·5–89°, occur in the wax from American Cotton (J. Text. Inst. 1924, **15**, 337T : Abstr. J.C.S. **128**, i, 879).

B. UNSATURATED ALCOHOLS

1. OLEFINE ALCOHOLS, $C_nH_{2n-1}.OH$

These are derived from the unsaturated olefines, C_nH_{2n}, in the same manner as the normal alcohols are obtained from their hydrocarbons. In addition to the general character of alcohols, they possess the property of the olefines to form addition compounds.

The chief representative of the class is allyl alcohol, $CH_2{=}CH{\cdot}CH_2OH$. When oxidized by potassium permanganate, the double linkage of the allyl alcohols is severed, and trihydric alcohols—glycerols—result (Ber. **21**, 3347).

Vinyl alcohol, $CH_2:CHOH$, separates as a mercury oxychloride compound, $C_2H_3O_2Hg_3Cl_2$, when ethyl ether, in which it is always present in small amount, is treated with an alkaline mercury oxychloride solution (Ber. **22**, 2863). It is produced simultaneously with hydrogen peroxide when ether is oxidized with atmospheric oxygen. It cannot be isolated from its mercury derivative, as all reactions which might be expected to produce it yield the isomeric acetaldehyde, $CH_3{\cdot}CHO$. Compounds containing the grouping $>C:CHOH$ tend to change to the tautomeric form $>CH{\cdot}CHO$ (Erlenmeyer sen., Ber. **13**, 309: **14**, 320). The monohalogenethylenes can be regarded as the halogen derivatives of vinyl alcohol.

Bromovinyl alcohol and the *dibromo compound*, $CHBr:CHOH$ and $CBr_2:CHOH$, are obtained as acetates by removing bromine from the addition product of di- and tribromoacetaldehydes and acetyl bromide by finely divided copper (Ber. **45**, 645).

$$CHBr_2CHBr{\cdot}O{\cdot}COCH_3 \longrightarrow CHBr:CHO{\cdot}COCH_3.$$

Allyl alcohol [*Propenol*-3], $C_3H_5{\cdot}OH = CH_2:CH{\cdot}CH_2{\cdot}OH$.—Allyl compounds occur in the vegetable kingdom: allyl sulphide and diallyl trisulphide (C. 1892, II. 833), in oil of garlic, and allyl thiocyanate, $C_3H_5{\cdot}NCS$, in oil of mustard. It may be prepared (1) by heating allyl iodide—which is easily prepared from glycerol—to 100° with 20 parts water; (2) it is produced, also, when nascent hydrogen acts on acrolein, $CH_2:CH{\cdot}CHO$, and (3) sodium on dichlorhydrin, $CH_2Cl{\cdot}CHCl{\cdot}CH_2OH$ (Ber. **24**, 2670). (4) It is best obtained from glycerol by heating the latter with oxalic acid.

The mechanism of the reaction between glycerol and oxalic acid is discussed later, in connection with the preparation of formic acid (see p. 282).

Properties.—Allyl alcohol is a mobile liquid with a pungent odour; it is miscible with water, and burns with a bright flame. Solidifies $-50°$, b.p. 96–97°, D^{20} 0·854.

It yields acrolein and acrylic acid when oxidized with silver oxide, and only formic acid (no acetic) with chromic acid. Glycerol results when potassium permanganate is the oxidant (Ber. **21**, 3351). Nascent hydrogen attacks it with difficulty, as seems to be indicated by its formation from acrolein. Boiling with zinc and sulphuric acid (Ber. **7**, 856), however, or with aluminium and potassium hydroxide solution (C. 1899, II. 181), or leading its vapour over finely divided nickel (C. 1907, II. 30), causes the formation of *n*-propyl alcohol; reduction with sodium-ammonium yields propylene (C. 1906, II. 670). Chlorine acts partly as an oxidizing, and partly as an additive reagent, giving rise to acrolein and dichlorhydrin (Ber. **24**, 2670). When heated to 150° with potassium hydroxide, formic acid, *n*-propyl alcohol, and other products are formed.

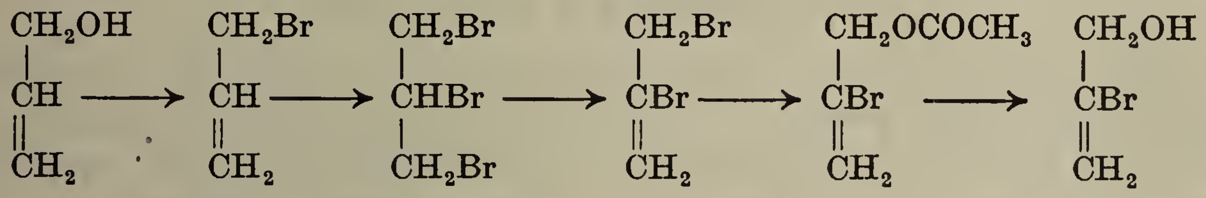
Allyl alcohol, when heated with mineral acids, yields propionic aldehyde and methyl ethyl acrolein (Ber. **20**, R. 699).

Mercuric salts form compounds with it, which dissolve with difficulty (Ber. **33**, 2692).

Halogen-substituted allyl alcohols have been obtained from α- and β-dichloropropylene and β-dibromopropylene.

α-Chlorallyl alcohol, $CH_2{=}CCl{\cdot}CH_2OH$, b.p. 136°.
β-Chlorallyl alcohol, $CHCl{=}CH{\cdot}CH_2OH$, b.p. 153°.
α-Bromallyl alcohol, $CH_2{=}CBr{\cdot}CH_2OH$, b.p. 152°.

Sulphuric acid, acting on α-chlorallyl alcohol, produces acetone-alcohol (*q.v.*), and with α-bromallyl alcohol yields propargyl alcohol (see p. 152). α-Bromallyl alcohol may be prepared from allyl alcohol by a series of reactions, shown in the following diagram :



β-*Allyl alcohol*, $CH_2{=}C(OH){\cdot}CH_3$, is only known in the form of its ether (p. 158). The *sodium* derivative is produced by the action of metallic sodium upon acetone (Ann. **278**, 116), diluted with anhydrous ether.

Crotonyl alcohols, C_4H_7OH.

Allylcarbinol (*Δ^{γ}-α-Butenol*) $CH_2 : CH{\cdot}CH_2{\cdot}CH_2OH$, b.p. 113°, is obtained by the action of magnesium allyl bromide on trioxymethylene (Compt. rend. **148**, 849).

α-*Methylallyl alcohol* (*Δ^{γ}-β-Butenol*) $CH_2 : CH{\cdot}CHOH{\cdot}CH_3$, b.p. 97°, is obtained by the action of magnesium methyl iodide on acrolein (Ber. **41**, 3621).

Crotonyl alcohol (*Δ^{β}-α-Butenol*) $CH_3{\cdot}CH : CH{\cdot}CH_2OH$, b.p. 117–120°, is obtained by the reduction of crotonaldehyde.

The **higher olefine alcohols** are synthetically prepared by means of the zinc and magnesium organic compounds (p. 220) : (1) from olefine aldehydes and zinc alkyls or magnesium alkyl halides (Ber. **37**, 3578 : **41**, 2739 : **43**, 1574, 2330 : **45**, 625 : C. 1908, I. 2225 ; II. 1677) ; or (2) from aldehydes or ketones with zinc and allyl iodide (Ber. **17**, R. 316 : **27**, 2434 : Ann. **185**, 151, 175 : **196**, 109 : J. pr. Chem. [2] **30**, 399 : C. 1901, I. 668, 997 : II. 622 : 1907, I. 96) or magnesium and allyl bromide (Ber. **42**, 435 : C. 1909, I. 1744 : 1912, I. 1441). (3) Many aldehydes and ketones, when boiled with acid chlorides, especially benzoyl chloride, yield the benzoic ester of the olefine alcohols isomeric with the ketones, *e.g.* $C_5H_{11}{\cdot}CH : CHO{\cdot}COC_6H_5$ from œnanthic aldehyde (p. 238) and benzoyl chloride ; $C_9H_{10}C(: CH_2)O{\cdot}COC_4H_9$ from methyl nonyl ketone and valeryl chloride (C. 1903, I. 71.) (4) αβ-olefine carboxylic esters are reduced by sodium and alcohol to saturated alcohols (see 4*d*, p. 131) ; on the other hand, carboxylic esters containing a remote olefine group, as in the case of allyl acetic acid, oleic acid, undecylic acid ester, etc., yield the corresponding olefine alcohols when similarly reduced (C. 1905, I. 25 : II. 1700). (5) From hydroxyalkylamines by exhaustive methylation followed by decomposition of the hydroxyalkyl ammonium hydroxide (D.R.P. 233519 : C. 1911, I. 1333).

Pentenols.

Δ^{γ}-β-Pentenol, $CH_3CH : CH{\cdot}CHOH{\cdot}CH_3$, b.p. 121°, is obtained from crotonaldehyde and magnesium methyl iodide. The corresponding hexenol and heptenol are obtained by the use of magnesium ethyl and propyl bromides (Ber. **39**, 1603).

Δ^{δ}-α-Pentenol, $CH_2 : CH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2OH$, b.p. 142°, is obtained by reduction of allylacetic ester.

Δ^{δ}-β-Pentenol, $CH_2 : CH{\cdot}CH_2{\cdot}CHOH{\cdot}CH_3$, b.p. 115°, is obtained from magnesium allyl bromide and acetaldehyde (Compt. rend. **154**, 710).

Hexenol. *Dimethylallylcarbinol*, b.p. 119·5°.

Octenols. *Diethylallylcarbinol*, b.p. 156°. *Methylpropylallylcarbinol*, b.p. 159–160°.

Nonenol. *βζ-Dimethyl-Δ^{ϵ}-hepten-β-ol.* $CMe_2 : CH{\cdot}[CH_2]_2CMe_2OH$, b.p. 79°/10 mm., from geraniol (C. 1898, II. 11).

Δ^{κ}-α-Undecenol. $CH_2 : CH{\cdot}[CH_2]_8{\cdot}CH_2OH$, m.p. −1°, b.p. 133°/13 mm. (Helv. Chem. Acta, **9**, 1074 : Ber. **55**, 2208) and **oleyl alcohol** (*Octadecenol*), $C_{18}H_{35}OH$, b.p. 207°/13 mm., are obtained from undecenoic ester and oleic ester by reduction.

Phytol is an alcohol, $C_{20}H_{39}OH$, which occurs as ester in chlorophyll (see Vol. III). Its constitution has been shown by synthesis to be

$$CHMe_2{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CMe : CH{\cdot}CH_2OH.$$

(Ann. **418**, 121 : **464**, 69 : **475**, 183 : *cf.* J.C.S. **1929**, 883).

2. ALCOHOLS, $C_nH_{2n-3}OH$

The alcohols of the above general formula comprise (I) alcohols containing a triple bond and (II) alcohols containing two double bonds. The best known of the former class is propargyl alcohol ; numerous representatives of the latter have been prepared synthetically, and also occur naturally in various ethereal oils.

I. Acetylene Alcohols

Propargyl alcohol [*Propinol*-3], $CH \vdots C{\cdot}CH_2OH$, b.p. 114°, $D_{20} = 0{\cdot}9715$.—This alcohol was obtained by Henry in 1872 (Ber. **5**, 569 ; **8**, 389) upon treating α-bromallyl alcohol (see p. 151) with potassium hydroxide. It is a mobile, agreeable-smelling liquid. Like acetylene, it forms an explosive *silver* compound, $C_3H_2(OH)Ag$, white in colour. The *copper* salt $(C_3H_2OH)_2Cu$, is a yellow precipitate.

Propargylcarbinol, $CH \vdots C{\cdot}CH_2{\cdot}CH_2OH$, b.p. 133–136°, is obtained from β-bromo-Δ^{α}-δ-butenol (C. 1908, II. 32). *Methyl-* and *ethylacetylenylcarbinols*, $CH \vdots C{\cdot}CHOH{\cdot}R$, b.pp. 108° and 125°, are obtained by the action of potassium hydroxide on the alcohols $CH_2 : CBr{\cdot}CHOH{\cdot}R$, obtained from α-bromoacrolein and the appropriate alkyl magnesium compound (C. 1911, I. 1578).

Homologous acetylene alcohols result from the action of sodium compounds of the alkyl acetylenes on trioxymethylene or other aldehydes (C. 1902, I. 629) :

$$RC \vdots CNa + R'{\cdot}CHO = RC \vdots CCH(ONa)R'.$$

The acetylene magnesium halides similarly react with aldehydes and ketones to form acetylenic alcohols (Bull. [3] **28**, 922 : C. 1909, II. 182).

Tertiary acetylene alcohols are obtained by the action of acetylene on the sodium derivative of the enolic forms of ketones (*Merling*, C. 1914, II. 1370 : Ber. **55**, 2903 : Ann. **442**, 72) :

$$CH_3{\cdot}C(ONa) : CH_2 + CH \vdots CH \longrightarrow CH_3{\cdot}C(ONa)Me{\cdot}C \vdots CH.$$

II. Diolefine Alcohols

Higher alcohols containing two double bonds are synthetically produced by the action of zinc and allyl iodide on esters of fatty acids (Ann. **197**, 70).

Diallylcarbinol, $(CH_2 : CH{\cdot}CH_2)_2CHOH$, b.p. 151°. *Diallylmethylcarbinol*,

$(CH_2:CH{\cdot}CH_2)_2$, $C(CH_3)OH$, b.p. 158°. *Diallylethylcarbinol,* $(CH_2:CH{\cdot}CH_2)_2$-$C(C_2H_5)OH$, b.p. 175°. *Diallylpropylcarbinol,* $(CH_2:CH{\cdot}CH_2)_2C(C_3H_7)OH$, b.p. 194° (C. 1901, I. 997).

Diolefine alcohols, which can be converted into terpenes, are of great theoretical interest; such are geraniol or rhodinol, and linalool. They will be discussed under the olefinic terpene or terpenogen group (Vol. II).

3. ALCOHOLS, $C_nH_{2n-5}OH$

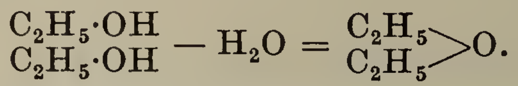
Alcohols containing three double bonds have been obtained by the action of zinc and allyl iodide on halogen-fatty esters (C. 1909, I. 268).

Triallylcarbinol, $(CH_2:CH{\cdot}CH_2)_3COH$, b.p. 191°, from chloroformic ester, zinc and allyliodide.

ALCOHOL DERIVATIVES

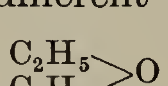
1. SIMPLE AND MIXED ETHERS

Ethers are the *oxides of the alcohol radicals.* If the alcohols are compared with basic hydroxides, then the ethers are analogous to the metallic oxides. They may be considered also as anhydrides of the alcohols, formed by the elimination of water from two molecules of alcohol :



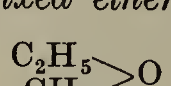
$$\begin{matrix}C_2H_5\cdot OH\\ C_2H_5\cdot OH\end{matrix} - H_2O = \begin{matrix}C_2H_5\\ C_2H_5\end{matrix}\!>O.$$

Ethers containing two similar alcohol radicals are termed *simple ethers* ; those with different radicals, *mixed ethers* :



$$\begin{matrix}C_2H_5\\ C_2H_5\end{matrix}\!>O$$

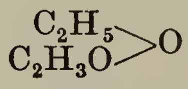
Ethyl ether, or diethyl ether.



$$\begin{matrix}C_2H_5\\ CH_3\end{matrix}\!>O$$

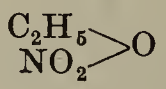
Methyl ethyl ether.

We must make a distinction between the above and the *esters* (formerly referred to as compound ethers), in which both an alcohol radical and an acid radical are present—*e.g.* :



$$\begin{matrix}C_2H_5\\ C_2H_3O\end{matrix}\!>O$$

Ethyl acetate ; and



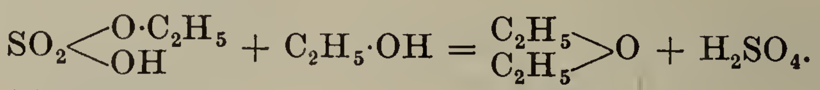
$$\begin{matrix}C_2H_5\\ NO_2\end{matrix}\!>O$$

Ethyl nitrate.

The properties of these substances are entirely different from those of the ethers, and in the following pages they will always be termed esters.

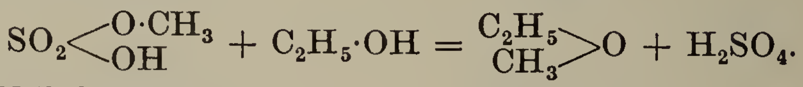
The following are the more important methods of preparing the ethers :

1. The chief method of formation consists of the interaction of sulphuric acid and alcohols. Alkyl hydrogen sulphates result at first, but on further heating with alcohols these are converted into ethers. This procedure affords a means of obtaining both simple and mixed ethers (*Williamson, Chancel*) :



$$SO_2\!<\!\begin{matrix}O\cdot C_2H_5\\ OH\end{matrix} + C_2H_5\cdot OH = \begin{matrix}C_2H_5\\ C_2H_5\end{matrix}\!>O + H_2SO_4.$$

Ethyl hydrogen sulphate. — Diethyl ether.



$$SO_2\!<\!\begin{matrix}O\cdot CH_3\\ OH\end{matrix} + C_2H_5\cdot OH = \begin{matrix}C_2H_5\\ CH_3\end{matrix}\!>O + H_2SO_4.$$

Methyl hydrogen sulphate. — Methyl ethyl ether.

When a mixture of two alcohols reacts with sulphuric acid, three ethers are simultaneously formed ; two are simple and one is a mixed ether. Subsidiary reactions give rise to the production of sulphones and sulphonic acids (C. 1897, II. 340 : 1899, II. 30). Other polybasic acids, such as phosphoric, arsenic, and boric, behave like sulphuric acid. This is also true of hydrochloric acid at 170°, and sulpho-acids—*e.g.* benzenesulphonic acid, at 145° (*F. Krafft*, Ber. **26**, 2829). In this reaction ethyl benzenesulphonate is produced and breaks down according to the equations :

$$C_6H_5SO_3H + C_2H_5OH = C_6H_5SO_3C_2H_5 + H_2O.$$
$$C_6H_5SO_3C_2H_5 + C_2H_5OH = C_6H_5SO_3H + (C_2H_5)_2O.$$

The dialkyl sulphates and methionates (Ann. **418**, 200) are converted by alcohols into ethers much more quickly than the alkyl sulphuric acids (C. 1907, I. 702).

Ethers generally can be obtained in good yield by passing the vapour of the alcohol over dried alum at 189–195° (Bull. Soc. Chim. [4] **25**, 565 : **27**, 121).

2. The action of the alkyl halides on the sodium alcoholates in alcoholic solution produces mixed ethers.

$$C_2H_5{\cdot}ONa + C_2H_5Cl = C_2H_5{\cdot}O{\cdot}C_2H_5 + NaCl.$$
$$C_2H_5{\cdot}ONa + C_3H_7Cl = C_2H_5{\cdot}O{\cdot}C_3H_7 + NaCl.$$

Consult Ber. **22**, R. 381, 637, upon the velocity of these reactions.

3. Halogen-substituted ethers yield homologous ethers on reaction with zinc or magnesium organic compounds, *e.g.* bromomethyl amyl ether (p. 221) and ethyl magnesium bromide yield amyl propyl ether (C. 1904, I. 1195) :

$$C_5H_{11}OCH_2Br + BrMgC_2H_5 = C_5H_{11}OC_3H_7 + MgBr_2.$$

4. Action of the alkyl halides on metallic oxides, especially silver oxide :

$$2C_2H_5I + Ag_2O = (C_2H_5)_2O + 2AgI$$

This indicates the constitution of the ethers.

Properties.—Ethers are neutral, volatile (hence the name *αἰθήρ*, air) bodies, nearly insoluble in water. The lowest members are gases ; the next higher are liquids, and the highest—*e.g.* cetyl ether—are solids. Their boiling points are very much lower than those of the corresponding alcohols (Ann. **243**, 1).

Reactions.—Ethers are very indifferent chemically, because all the hydrogen is attached to carbon.

(1) When oxidized they yield the same products as their alcohols.

(2) They yield esters when heated with concentrated sulphuric acid.

(3) Phosphorus pentachloride converts them into alkyl chlorides :

$$C_2H_5{\cdot}O{\cdot}CH_3 + PCl_5 = C_2H_5Cl + CH_3Cl + POCl_3$$

(4) The same occurs when they are heated with the halogen acids, especially with HI at 100° (C. 1897, II. 408 ; 1901, II. 679) :

$$C_2H_5{\cdot}O{\cdot}CH_3 + 2HI = C_2H_5I + CH_3I + H_2O.$$

In the cold the effect of the HI is to cause decomposition into alcohol and iodide, and in the case of mixed methyl alkyl ethers the production of methyl iodide and the higher alcohol predominates. If the alkyl group is a tertiary one, the *tert.*-alkyl iodide mainly is produced ; but in other cases a mixture of the two possible iodides and alcohols results (Ber. **39**, 2569).

$$C_2H_5{\cdot}O{\cdot}CH_3 + HI = CH_3I + C_2H_5OH.$$

Zeisel's method for the estimation of methoxy- and ethoxy-groups in a compound depends upon this splitting off of methyl or ethyl iodide when such compounds are heated with concentrated hydriodic acid (see p. 11).

(5) Many ethers, especially those containing secondary and tertiary, or unsaturated groups, are broken down into alcohols when heated with water or very dilute sulphuric acid at 150° (Ber. **10,** 1903); *e.g.* vinyl ethyl ether decomposes into alcohol and aldehyde (Ber. **39,** 1410 footnote).

(6) Ether combines with many substances to form addition compounds, as, for example, with magnesium or zinc iodide, magnesium alkyl halides (p. 230) producing bodies of the type $2R_2O{\cdot}MgI_2$, $R_2O{\cdot}MgIR'$, etc. This is due to the formation of a tetravalent oxonium oxygen atom (*Baeyer* and *Villiger*, Ber. **34,** 2688).

With benzoyl chloride (Vol. II) the ether magnesium iodide breaks up into ethyl iodide, ethyl benzoate and $MgCl_2$ (C. 1905, I. 1082: Ber. **38,** 3665):

$$2(C_2H_5)_2O{\cdot}MgI_2 + 2C_6H_5COCl = 2C_2H_5I + 2C_6H_5CO{\cdot}OC_2H_5 + MgCl_2.$$

A. ETHERS OF THE SATURATED ALCOHOLS

Methyl ether, $(CH_3)_2O$, is prepared by heating methyl alcohol with sulphuric acid (Ber. **7,** 699). It is an agreeable-smelling gas, which may be condensed to a liquid at about − 23°. Water dissolves 37 volumes and sulphuric acid upwards of 600 volumes of the gas.

Chlorine converts methyl ether into chloromethyl ether, *sym.*-dichloromethyl ether, and perchloromethyl ether which partially decomposes on boiling. The first two, together with the corresponding bromo- and iodo-compounds, will be treated later as derivatives of formaldehyde.

Ethyl ether or **Ether,** $(C_2H_5)_2O$, is by far the most important representative of this class of compounds. It has been known for a long time.

History.—Ethyl ether and its production from alcohol and sulphuric acid were known and described by Valerius Cordus, a German physician, in the sixteenth century. Until the beginning of the last century ether was regarded as a sulphur-containing body; hence, to distinguish it from other ethereal compounds, it was called *sulphuric ether.* The ether process, in which a comparatively small quantity of sulphuric acid was capable of converting a large quantity of alcohol into ether, was included in the category of catalytic reactions. The explanation of this process constitutes one of the most important advances in organic chemistry.

In 1842, *Gerhardt,* from purely theoretical reasons and in opposition to *Liebig,* concluded that the ether molecule did not contain the same number of carbon atoms as were present in the alcohol molecule, but *twice* that number. He was unable to gain general acceptance for this view. *Williamson,* in 1850, by a new synthesis of ether, proved the correctness of Gerhardt's conception, not only for it, but for ethers in general; he caused reaction to take place between sodium ethoxide and ethyl iodide (p. 164). The formation of ether from alcohol and sulphuric acid Williamson explained by a continuous breaking-down and re-formation of ethyl sulphuric acid, made possible by the contact of alcohol with the acid at 140° (Ann. **77,** 37; **81,** 73).

Chancel, whom Williamson preceded in publication, had made ether independently, by heating a mixture of potassium ethyl sulphate and potassium ethoxide:

$$SO_4\left\{\begin{matrix}C_2H_5\\K\end{matrix}\right. + O\left\{\begin{matrix}C_2H_5\\K\end{matrix}\right. = SO_4\left\{\begin{matrix}K\\K\end{matrix}\right. + O\left\{\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right.$$

The objection that ether, because of its low boiling temperature, could not contain the double number of carbon atoms in its molecule, Chancel removed by citing the boiling point of ethyl acetate (*Laurent* and *Gerhardt*, Compt. rend., 1850, **6**, 369).

Ethyl alcohol	C_2H_5OH	b.p. 78°.
Ether	$(C_2H_5)_2O$	b.p. 35°.
Acetic acid	CH_3CO_2H	b.p. 118°.
Ethyl acetate	$CH_3CO_2C_2H_5$	b.p. 77°.

Preparation.—Ether is made (1) from ethyl alcohol and sulphuric acid heated to 140°. The process is continuous. (2) From benzenesulphonic acid and alcohol at 135–145° (Ber. **26**, 2829).

The advantage in the second method is that the ether is not contaminated with sulphur dioxide, which in the first method has to be removed from the crude product by washing with a soda solution. Anhydrous ether may be obtained by distilling ordinary ether over quick-lime, and drying it finally with sodium until there is no further evolution of hydrogen.

Test for Water and Alcohol.—When ether containing water is shaken with an equal volume of CS_2, a turbidity results. When alcohol is present, the ether, on shaking with aniline violet, is coloured; anhydrous ether does not acquire a colour when similarly treated.

Properties.—Ethyl ether is a mobile liquid with a characteristic odour. It boils at 34·5° and melts at − 113°, D^{15}_{15} 0·71994. It dissolves in 10 parts of water and is miscible with alcohol. Many carbon compounds insoluble in water, such as the fats and resins, are soluble in ether. It is extremely inflammable, burning with a luminous flame. Its vapour forms a very explosive mixture with air. When inhaled, ether vapour brings about unconsciousness, a property discovered in 1842 by *Charles Jackson*, of Boston, and has been used in surgery since *Morton's* employment of it in 1846. *Hoffmann's Anodyne, Spiritus Ætherеus* (so named after the great Halle clinician, who died in 1742) is a mixture of 3 parts alcohol and 1 part ether.

Ether unites with bromine to form peculiar, crystalline addition products somewhat like the so-called bromine hydrate; it combines, too, with water, metallic salts, hydroferrocyanic acid, etc. (see above, p. 156).

Vinyl alcohol (*q.v.*) and hydrogen peroxide are produced in small quantity by the action of air on moist ether. By the slow combustion of ether, formaldehyde peroxide $HOCH_2O·OCH_2OH$ is produced (Ber. **29**, R. 840: *cf.* Ber. **38**, 1409). When ozone is passed into anhydrous ether an explosive peroxide is formed. With water and sulphuric acid at 180°, ether is broken down again to ethyl alcohol.

Halogen derivatives of ethyl ether.—Chlorine acts on cooled ether to produce the following substitution products: (Ann. **279**, 301):

Monochloroether,	$CH_3·CHCl·O·C_2H_5$,	b.p. 98°.
αβ-Dichloroether,	$CH_2Cl·CHCl·O·C_2H_5$,	b.p. 145°.
Trichloroether,	$(CHCl_2·CHCl·O·C_2H_5$,	b.p. 170–175° (C. 1904, I. 920).
Perchloroether,	$(C_2Cl_5)_2O$,	m.p. 68°.

The last of these, perchloroether, breaks down on distillation into hexachloroethane and trichloroacetyl chloride.

The α-halogen derivatives of the general type $CH_3CHX·O·C_2H_5$ are described later, with the aldehyde alcoholates, and the β-derivatives $CH_2X·CH_2·O·C_2H_5$ are the ethers of the glycol halogenohydrins.

Homologous ethers.

The following table contains the melting and boiling points of the better-known simple and mixed ethers :

Methyl ethyl ether	b.p. 11°	*Methyl* n-*propyl ether*	b.p. 37°
Methyl tert.-*butyl ether*	b.p. 54°	*Methyl* iso*propyl ether*	b.p. 32°
n-*Propyl ether*	b.p. 90°	iso*Propyl ether*	b.p. 70°
Ethyl tert.-*butyl ether*	b.p. 70°	iso*Propyl* tert.-*butyl ether*	b.p. 75°
iso*Amyl ether*	b.p. 160°	*Cetyl ether* $(C_{16}H_{33})_2O$, m.p. 55°	b.p. 300°

The majority of these ethers are produced by the interaction of alkyl halides and sodium alcoholates (C. 1903, I. 119 : 1904, I. 1065) ; *n*-propyl ether is formed from propyl alcohol and ferric chloride, at 145–155° (C. 1904, II. 18). *Methyl* tert.-*amyl ether*, $(OH_3)_2C(OCH_3)\cdot CH_2CH_3$, b.p. 86°, is prepared from trimethyl ethylene by heating it with methyl alcohol and iodomethane (C. 1907, I. 1125).

B. ETHERS OF UNSATURATED ALCOHOLS

It was explained, when discussing the unsaturated alcohols (p. 150), that the members of that series in which hydroxyl was combined with a doubly linked carbon atom readily rearranged themselves into aldehydes or ketones, and were only known in their derivatives, especially as ethers. Thus :

Vinyl ether, $(CH_2{=}CH)_2O$, b.p. 39°, may be obtained from vinyl sulphide (p. 173) and silver oxide. *Perchlorovinyl ether, Chloroxethose* $(CCl_2{=}CCl)_2O$, is formed from perchloroethyl ether (above) and K_2S. *Vinyl ethyl ether*, b.p. 35·5°, results from the interaction of iodoethyl ether and sodium ethoxide ; also from acetal by P_2O_5 and quinoline (Ber. **31**, 1021). It has been obtained recently by passing acetylene into a mixture of alcohol and sulphuric acid at 0° (C. 1921, II. 645).

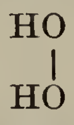
αβ-Dichlorovinyl ethyl ether, $CHCl : CCl\cdot OEt$, b.p. 128°, from trichloroethylene and sodium ethylate, yields, when heated with water containing some HCl, ethyl chloroacetate (J.C.S. **117**, 691) : the products obtained by the addition of hydrogen chloride or chlorine to this ether break down on distillation into chloroacetyl and dichloroacetyl chlorides respectively (Chem. Ztg. **35**, 1053). *ββ-Dichlorovinyl ethyl ether*, $CCl_2 : CH\cdot OEt$, b.p. 145°, from tetrachloroethyl ether (p. 244) and zinc, passes by uptake of oxygen into ethoxychloroacetyl chloride, $EtOCHCl\cdot COCl$ (J.A.C.S. **31**, 412, 596). *Dibromovinyl ethyl ether*, b.p. 169°, is oxidized by nitric acid to dibromoacetic ester (Ann. **298**, 334 : Ber. **46**, 143). iso*Propenyl ethyl ether*, $CH_3C(OC_2H_5){=}CH_2$, b.p. 62–63°, is formed from propenyl bromide and alcoholic potassium hydroxide, and from ethoxycrotonic acid (Ber. **29**, 1005). The homologues of *β*-alkoxyacrylic acid also easily part with CO_2 and yield the homologous *alkoxyethylenes*, $RC\cdot(OC_2H_5) : CHR'$; these all yield ketones and alcohols when hydrolysed with dilute acids (C. 1904, I. 719 : Ber. **39**, 1410 footnote).

Allyl ether, $(CH_2{=}CH\cdot CH_2)_2O$, b.p. 85° ; *Ethyl Δ^{γ}-butenyl ether*, $CH_2 : CH\cdot CH_2\cdot CH_2\cdot OEt$, b.p. 90° (Compt. rend. **150**, 1056).

Propargyl ethyl ether, $CH{\equiv}C\cdot CH_2\cdot O\cdot CH_2\cdot CH_3$, b.p. 80°.

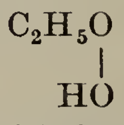
ALKYL HYDROGEN AND DIALKYL PEROXIDES

The alkyl hydrogen peroxides and the dialkyl peroxides stand in the same relation to hydrogen peroxide, as the monohydric alcohols and the ethers do to water :



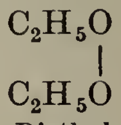
$$\begin{matrix} HO \\ | \\ HO \end{matrix}$$

Hydrogen peroxide.



$$\begin{matrix} C_2H_5O \\ | \\ HO \end{matrix}$$

Ethyl hydrogen peroxide.



$$\begin{matrix} C_2H_5O \\ | \\ C_2H_5O \end{matrix}$$

Diethyl peroxide.

Ethyl hydrogen peroxide and diethyl peroxide are the only members which have been closely studied. They result from the interaction of diethyl sulphate and a 12 per cent. solution of hydrogen peroxide, and the subsequent slow addition of potassium hydroxide solution during continuous shaking. An excess of hydrogen peroxide favours the production of ethyl hydrogen peroxide (*Baeyer* and *Villiger*, Ber. **34**, 738).

Ethyl hydrogen peroxide, $C_2H_5O\cdot OH$, is a colourless liquid, which can be distilled without decomposition, between 26° and 47° at 100 mm. pressure. It is miscible with water, alcohol, and ether, and can be separated out from its aqueous solution by the addition of ammonium sulphate and potassium carbonate. Its odour is that of bleaching powder and acetaldehyde together. A drop of the concentrated solution on the skin causes inflammation. When rapidly heated, it detonates, and a strong explosion occurs when it is brought into contact with very finely divided silver. Acyl derivatives of hydrogen peroxide result from interaction with carboxylic anhydrides. Tertiary bases are oxidized to amine oxides by ethyl hydroperoxide.

Barium salt, $(C_2H_5OO)_2Ba + 2H_2O$, is formed by dissolving barium hydroxide in an aqueous solution of ethyl hydrogen peroxide. It crystallizes as a leafy mass.

Diethyl peroxide, $CH_3CH_2{\cdot}O{\cdot}O{\cdot}CH_2CH_3$, b.p. 65°, $D_4^{15} = 0{\cdot}8273$. It is slightly soluble in water, but soluble in alcohol and ether. On contact with a thermometer heated to 250° it burns rapidly but without noise. If the liquid, in a CO_2 atmosphere, is approached by a heated copper wire which is then removed, it disappears very quickly without generation of light or boiling ; this phenomenon is looked on as being a slow explosion. The products of combustion consist of formaldehyde and CO, together with some ethane.

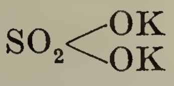
2. ESTERS OF THE MINERAL ACIDS

If we compare the alcohols with the metallic bases, the esters or compound ethers (p. 154) are perfectly analogous in constitution to the salts. Just as salts result from the union of metallic hydroxides with acids, so esters are formed by the combination of alcohols with acids, water being formed in both reactions :

$$NaOH + HCl = NaCl + H_2O.$$
$$C_2H_5OH + HCl = C_2H_5Cl + H_2O.$$

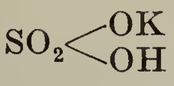
The haloid esters correspond to the haloid salts ; they may also be regarded as monohalogen substitution products of the hydrocarbons (p. 120). Corresponding with the oxygen salts are the esters of other acids, which, therefore, may be viewed as derivatives of the alcohols, in which the alcohol-hydrogen has been replaced by acid radicals, or as derivatives of the acids, in which the hydrogen replaceable by metals has been substituted by alcohol radicals. The haloid esters are included in the last definition of esters.

In polybasic acids all the hydrogen atoms can be replaced by alcoholic radicals, whereby *neutral esters* are produced. When all the hydrogen atoms are not replaced by alcoholic radicals, *alkyl hydrogen esters* are formed, which still possess the acid character. They form salts, hence are termed *ester acids,* and correspond with acid salts :



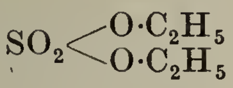
$$SO_2<\begin{matrix}OK\\OK\end{matrix}$$

Potassium sulphate.



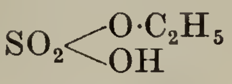
$$SO_2<\begin{matrix}OK\\OH\end{matrix}$$

Potassium hydrogen sulphate.



$$SO_2<\begin{matrix}O{\cdot}C_2H_5\\O{\cdot}C_2H_5\end{matrix}$$

Ethyl sulphate.



$$SO_2<\begin{matrix}O{\cdot}C_2H_5\\OH\end{matrix}$$

Ethyl hydrogen sulphate.

Dibasic acids thus form two series of salts and esters, whilst with tribasic acids there are three series of salts and esters.

In the case of the polyhydric alcohols there are, besides the neutral esters, also basic esters, corresponding with the basic salts, in which not all of the hydroxyl groups are esterified.

Formation of Esters.—(1) The esters can be prepared by direct combination of alcohols and acids, when water is also produced:

$$\text{Alcohol} + \text{Acid} \rightleftarrows \text{Ester} + \text{Water.}$$

This reaction is the classical example for the study of the Law of Mass Action. The change is never completed in the direction left --> right, but an equilibrium is reached, characteristic for each alcohol-acid mixture, and the same equilibrium is attained no matter whether we start with an equivalent mixture of alcohol and acid or with one of ester and water. If one of the products can be removed from the reacting mixture, then the change can go on to completion (see p. 310).

When acted on by alcohols, the polybasic acids mostly yield the alkyl hydrogen esters.

(2) By reacting on the silver or alkali salts of the acids with alkyl halides:

$$NO_2{\cdot}O{\cdot}Ag + C_2H_5I = NO_2{\cdot}O{\cdot}C_2H_5 + AgI.$$

(3) By acting on the alcohols or metallic alcoholates with acid chlorides:

$$2C_2H_5{\cdot}OH + SO_2Cl_2 = SO_2{<}^{O\cdot C_2H_5}_{O\cdot C_2H_5} + 2HCl.$$

$$3C_2H_5{\cdot}OH + BCl_3 = B(O{\cdot}C_2H_5)_3 + 3HCl.$$

Properties.—The neutral esters are insoluble, or soluble with difficulty in water, and almost all are volatile; therefore the determination of their vapour density is a convenient means of establishing the molecular magnitude and also the basicity of the acids. The ester acids are not volatile, but are soluble in water and yield salts with the bases.

All esters, and especially the ester-acids, are decomposed into alcohols and acids (p. 130) when heated with water. Sodium and potassium hydroxides, in aqueous or alcoholic solution, accomplish this with great readiness when heated. This process is termed *saponification* because the soaps—*i.e.* the potassium and sodium salts of the higher fatty acids (*q.v.*)—are obtained by this reaction from the fats, the glycerol esters:

$$NO_2{\cdot}O{\cdot}C_2H_5 + KOH = C_2H_5OH + NO_2OK.$$

A more general term for this process is *hydrolysis*.

A. I. ALKYL ESTERS OF THE HALOGEN ACIDS, ALKYL HALIDES

It was pointed out under the halogen substitution products of the paraffins and the unsaturated acyclic hydrocarbons that the *mono*-substitution products, or *alkyl halides*, were mostly prepared from the alcohols. As haloid esters of the alcohols they are discussed with the alkyl esters of the inorganic oxygen acids.

The view that the halogen derivatives $C_nH_{2n+1}X$ are paraffin substitution products is expressed in the names chloromethane, chloroethane, etc., whilst the designation methyl chloride, ethyl chloride, etc., for the monohalogen substitution derivatives of methane and ethane, mark these substances as haloid esters of the alcohols, corresponding with the metallic halides.

Formation and Preparation.—(1) *By the substitution of the paraffins.*

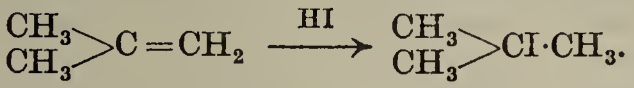
The conditions favouring the substitution of the hydrogen atoms of the paraffins by halogen atoms have been mentioned under the general methods for the preparation of halogen substitution products. The substitution reaction is not well adapted for the preparation of alkylogens, because mixtures of compounds are invariably produced, and among the higher members of the series isomers are formed. This is because the chlorine replaces the hydrogen both of terminal and intermediate carbon atoms (Ber. **39**, 2153). Thus normal pentane,

$$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3 \text{ yields } \begin{array}{l} CH_3{\cdot}CH_2{\cdot}CHCl{\cdot}CH_2{\cdot}CH_3 \text{ and} \\ CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CHCl{\cdot}CH_3, \\ CH_3CH_2CH_2CH_2CH_2Cl, \end{array}$$

and such mixtures are separated with great difficulty.

(2) *By the addition of halogen acids to the olefines.*—In this addition, which occurs with especial ease with hydriodic acid, the halogen atom, in general, attaches itself to the carbon atom carrying the least number of hydrogen atoms (p. 106):

$$CH_3{\cdot}CH{=}CH_2 \xrightarrow{HI} CH_3{\cdot}CHI{\cdot}CH_3.$$



$$\begin{matrix}CH_3\\CH_3\end{matrix}{>}C{=}CH_2 \xrightarrow{HI} \begin{matrix}CH_3\\CH_3\end{matrix}{>}CI{\cdot}CH_3.$$

In the case of propylene and hydriodic acid, some n-*propyl iodide* is also formed (*Michael*, Ber. **39**, 2138).

(3) *From alcohols* (*a*) *by the action of halogen acids.*—This reaction does not take place to completion unless the halogen acid is present in great excess, or the water formed simultaneously with the alkyl halide is removed by a dehydrating agent such as sulphuric acid or zinc chloride. The addition of dehydrating agents is not entirely safe with higher alcohols, as olefines are formed in the reaction, and combine with the halogen acid to give a halogen derivative isomeric with that expected. Tertiary alcohols are readily converted into their chlorides by hydrochloric acid.

In the case of hydriodic acid, the reducing character of the reagent has to be considered. If this acid is present in excess the products from various polyhydric alcohols are alkyl iodides (usually *sec.*-alkyl iodides), *e.g.*:

$$\begin{array}{l} C_2H_4(OH)_2 + 3HI = C_2H_5I + I_2 + 2H_2O. \\ C_3H_5(OH)_3 + 5HI = C_3H_7I + 2I_2 + 3H_2O. \\ C_4H_6(OH)_4 + 7HI = C_4H_9I + 3I_2 + 4H_2O. \\ C_6H_8(OH)_6 + 11HI = C_6H_{13}I + 5I_2 + 6H_2O. \end{array}$$

(*b*) *By the action of phosphorus halides.*—If, for example, ethyl alcohol be treated with PCl_3, PBr_3, or PI_3, two possibilities arise: either a halogen acid and ethyl ester of phosphorous acid are produced, or an ethyl halide and phosphorous acid. The latter reaction occurs when PBr_3 and PI_3 are used, and this method is adopted almost exclusively in the preparation of the alkyl bromides and iodides (see ethyl bromide and ethyl iodide):

$$\begin{array}{l} PBr_3 + 3C_2H_5OH = 3C_2H_5Br + H_3PO_3. \\ PI_3 + 3C_2H_5OH = 3C_2H_5I + H_3PO_3. \end{array}$$

(BI_3 acts analogously on ethyl alcohol, Ber. **24**, R. 387.) The formation of esters of phosphorous acid by the use of PBr_3 and PI_3 is far from satisfactory. PCl_3, on the other hand, yields phosphorous esters and hydrochloric acid almost entirely according to the equation (C. 1905, II. 1664; see p. 170):

$$PCl_3 + 3C_2H_5OH \longrightarrow P(OH)(OC_2H_5)_2 + C_2H_5Cl + HCl.$$

The chlorides are readily formed if PCl_5 be substituted for PCl_3:

$$PCl_5 + C_2H_5OH = C_2H_5Cl + HCl + POCl_3.$$

(c) *By the action of thionyl chloride or thionyl bromide*, in the presence of tertiary bases such as pyridine or dimethylaniline (Compt. rend. **152**, 1314):

$$C_5H_{11}OH + SOCl_2 + C_5H_5N \longrightarrow C_5H_{11}Cl + SO_2 + C_5H_5N{\cdot}HCl.$$

(4) *From alkyl sulphates and alkylsulphuric acids and metallic halides.*—Thus ethyl bromide is obtained from ethylsulphuric acid and potassium bromide, or more simply from a mixture of ethyl alcohol, sulphuric acid and potassium bromide. Similarly, methyl and ethyl sulphates react with alkali iodides in aqueous solution to yield the corresponding alkyl iodide.

(5) *From amines.*—The corresponding primary and secondary amines can be converted into alkyl halides by treating their benzoyl derivatives with phosphorus pentachloride or pentabromide, and distilling the benzamido- or benzimido-halide so formed (Ber. **44**, 1464):

$$R{\cdot}NH_2 \longrightarrow C_6H_5CO{\cdot}NHR \longrightarrow C_6H_5CCl:NR \longrightarrow C_6H_5CN + RCl.$$

(6) *Interconversion of alkyl halides.*—(*a*) Bromides and iodides can be transformed into chlorides by heating them with $HgCl_2$:

$$2C_3H_7I + HgCl_2 = 2C_3H_7Cl + HgI_2.$$

(*b*) When chlorides are heated with $AlBr_3$ or AlI_3 or CaI_2 they become converted into bromides or iodides (Ber. **14**, 1709: **16**, 392: **19**. R. 166):

$$3C_2H_5Cl + AlBr_3 = 3C_2H_5Br + AlCl_3.$$

(*c*) Methyl and ethyl iodides yield with AgF the gaseous compounds *methyl fluoride*, CH_3F, and *ethyl fluoride*, C_2H_5F, which have an agreeable, ethereal odour, and do not attack glass (Ber. **22**, R. 267).

(*d*) Chlorides and bromides are partly converted into iodides by heating with sodium iodide in acetone solution (Ber. **43**, 1528).

(*e*) Alkyl iodides are obtained from magnesium alkyl chlorides or bromides by the action of iodine (C. 1903, I. 318):

$$R{\cdot}MgCl + I_2 \longrightarrow R{\cdot}I + MgClI.$$

Isomerism.—Propane is the first hydrocarbon capable of yielding isomers (p. 35). The isomerism depends on the varying position of the hydrogen atoms in the same carbon chain, and from butane forward it also depends on the different linkage of the carbon atoms forming the carbon skeleton (see table, p. 163).

Properties and Reactions.—The alkyl halides are ethereal, agreeable, sweet-smelling liquids. They are scarcely soluble in water, but dissolve with ease in alcohol and ether. The lower members are gases at the ordinary temperature—*e.g.* methyl chloride, ethyl chloride, and methyl bromide. The chlorides boil 28–20° lower than the bromides, and the latter from 34–28° lower than the corresponding iodides (p. 163). The differences grow less with increasing molecular weight. As in the case of the paraffins, here also, where isomers exist, the normal members have the highest boiling points ; the more branched the carbon chain, the lower will the boiling point lie.

The alkyl halides differ from the metallic halides, to which in some ways they may be compared, in having the halogen linked by a covalency and not an electrovalency (see p. 30) and therefore do not react instantaneously with silver nitrate like the metallic halides. Of the alkyl halides, the iodides are the most reactive. The principal use of the alkyl halides is to introduce alkyl groups into organic molecules, generally by allowing them to act on metallic derivatives, when the metal is replaced by the alkyl group.

The reactions are of two main types, (1) where the entering alkyl group becomes directly attached to a carbon atom and thereby the carbon nucleus of the compound is altered and (2) where the alkyl group becomes attached to some element other than carbon.

Examples of type (1) are given by the reaction which takes place between an alkyl halide and the sodium derivative of malonic ester (*q.v.*) :

$$R\cdot I + CHNa(CO_2Et)_2 \longrightarrow NaI + CHR(CO_2Et)_2$$

and of type (2) in the reactions by which mercaptans and amines are formed :

$$R\cdot Br + KSH \longrightarrow \underset{\text{Mercaptan.}}{R\cdot SH} + KBr$$

$$R\cdot Cl + NH_3 \longrightarrow R\cdot NH_2,\ HCl.$$

They react under appropriate conditions with certain metals, such as zinc and magnesium with the formation of organometallic compounds (see p. 219) : with the alkali metals, halogen is removed, and two alkyl groups join together to produce a hydrocarbon (see p. 96).

The following table gives the boiling points of the more important alkyl halides at atmospheric pressure :

Radical.	Formula.	Chloride b.p.	Bromide b.p.	Iodide b.p.
Methyl	$CH_3\cdot$	− 24°	+ 4·5°	43°
Ethyl	$C_2H_5\cdot$	+ 12·5°	38°	72°
n-Propyl	$CH_3\cdot CH_2\cdot CH_2\cdot$	44°	71°	102°
*iso*Propyl	$(CH_3)_2CH\cdot$	36·5°	58·9°	89·5°
n-Butyl	$CH_3(CH_2)_3\cdot$	77·5°	100·4°	129·6°
*iso*Butyl	$(CH_3)_2\cdot CH\cdot CH_2\cdot$	68·5°	92°	120°
sec.-Butyl	$C_2H_5\cdot CH(CH_3)\cdot$	—	—	120°
tert.-Butyl	$(CH_3)_3C\cdot$	51·5°	74°	103·3°
n-Amyl	$CH_3\cdot(CH_2)_4\cdot$	106°	129°	155°
*iso*Amyl	$(CH_3)_2CH\cdot CH_2\cdot CH_2$	100°	120°	148°
Diethylcarbinyl·	$(C_2H_5)_2CH\cdot$	—	—	145°
Methylpropylcarbinyl	$C_3H_7\cdot CH(CH_3)\cdot$	104°	113°	144°
Methyl*iso*propylcarbinyl	$(CH_3)_2CH\cdot CH(CH_3)\cdot$	91°	115°	138°
Dimethylethylcarbinyl	$C_2H_5\cdot C(CH_3)_2\cdot$	86°	100°	127°
n-Hexyl	$CH_3(CH_2)_5\cdot$	133°	155°	179°
n-Heptyl	$CH_3\cdot(CH_2)_6\cdot$	159°	178°	203°
n-Octyl	$CH_3\cdot(CH_2)_7\cdot$	180°	199°	225°
		m.p.	m.p.	m.p.
Cetyl	$C_{16}H_{33}\cdot$	—	15°	22°
Myricyl	$C_{30}H_{61}\cdot$	64°	—	70°

Methyl fluoride, *Fluoromethane*, CH_3F, b.p. − 78°, is obtained according to method 6(*c*) (p. 162) or by heating tetramethylammonium fluoride (C. 1904, II. 1281).

Methyl chloride, *Chloromethane*, CH_3Cl, m.p. − 103° (Ber. **33**, 638), is obtained from methane or methyl alcohol. It is a sweet-smelling gas. Alcohol will dissolve 35 volumes of it, and water 4 volumes.

It is prepared by heating a mixture of 1 part methyl alcohol (wood spirit), 2 parts sodium chloride, and 3 parts sulphuric acid. A better plan is to conduct HCl into boiling methyl alcohol in the presence of zinc chloride (½ part). The disengaged gas is washed with KOH, and dried by means of sulphuric acid. Commercial methyl chloride is obtained by heating trimethylamine hydrochloride, $N(CH_3)_3{\cdot}HCl$, and is usually supplied in a compressed condition. It was formerly employed in the manufacture of the aniline dyes, and in producing cold.

Ethyl chloride, *Chloroethane*, C_2H_5Cl, b.p. 12·5°, $D_0 = 0{\cdot}921$. It is prepared from ethyl alcohol in the same manner that methyl chloride is obtained from its alcohol. Its formation from "ethyl hydride" or dimethyl by means of chlorine is important from a theoretical standpoint.

It is an ethereal liquid, miscible with alcohol, and but sparingly soluble in water: it is used as an anæsthetic.

If heated with water at 100° in a sealed tube, it changes to ethyl alcohol, a conversion which is accelerated by potassium hydroxide. In diffused sunlight, chlorine acts upon it to form ethylidene chloride, $CH_3{\cdot}CHCl_2$, and other substitution products. Chlorine, in the presence of iron, converts chloroethane into ethylene chloride.

Methyl bromide, *Bromomethane*, CH_3Br, b.p. + 4·5°, D_0 1·73 (Ber. **38**, 1865).

Ethyl bromide, *Bromoethane*, C_2H_5Br, b.p. 39°; $D_{13} = 1{\cdot}47$. It is prepared from potassium bromide and ethyl sulphuric acid (p. 168). It is used as a narcotic.

Propyl bromide, *α-Bromopropane*, C_3H_7Br, b.p. 71°; $D_{20} = 1{\cdot}3520$, is prepared from the normal alcohol (C. 1906, II. 1042).

*iso***Propyl bromide,** *β-Bromopropane*, C_3H_7Br, b.p. 59·5°; $D_{30} = 1{\cdot}3097$, is obtained from its corresponding alcohol. It is most conveniently prepared by the action of bromine on *iso*propyl iodide (Ber. **15**, 1904). On boiling with aluminium bromide, or by heating to 250°, normal propyl bromide is partially converted into *iso*propyl bromide (Ber. **16**, 391). Similarly, *iso*butyl bromide, $Me_2CH{\cdot}CH_2Br$, undergoes partial change on heating with formation of *tert.*-butyl bromide, $Me_2CBr{\cdot}CH_3$: this reaction is reversible, and the tertiary bromide at 240° is converted to the extent of 25% into the primary bromide. The obvious interpretation of these changes is to presume a primary decomposition of the bromide into hydrogen bromide and an olefine, with subsequent recombination according to the general rule: the change takes place, however, at a temperature at which no such dissociation is observed (Ann. **379**, 263: **393**, 81) and the assumption that the change is a real intramolecular reaction is supported by the change of chloro- and bromo-tetramethylmethane on distillation into the *tert.*-amyl halide, with migration of a methyl group,

$$(CH_3)_3C{\cdot}CH_2Br \longrightarrow (CH_3)_2CBr{\cdot}CH_2CH_3.$$

(Ann. Chim. Phys. [6] **29**, 359: [8] **21**, 341).

On exposure to the air the *iodides* soon become discoloured by liberation of iodine. The iodides of the secondary and tertiary alcohols are easily converted by heat into alkylenes, C_nH_{2n}, and HI. Consult Ann. **243**, 30, upon the specific volumes of the iodo-alkyls.

Methyl iodide, *Iodomethane*, CH_3I, b.p. 43°; $D_0 = 2{\cdot}19$, is prepared from methyl alcohol, iodine, and phosphorus, or from dimethyl sulphate and potassium iodide in aqueous solution (C. 1906, II. 1589). It is a heavy, sweet-smelling liquid, and unites with H_2O to form a crystalline hydrate, $2CH_3I + H_2O$, and with methyl alcohol to form a compound, $3CH_3I + CH_3OH$, b.p. 40°, without decomposition (C. 1901, II. 179).

At low temperatures the alkyl iodides take up chlorine, forming extremely easily decomposable iodochlorides:

Methyl iodochloride, CH_3ICl_2, m.p. − 28°, consists of yellow crystals. It decomposes into iodine chloride and chloromethane (Ber. **38**, 2842).

Ethyl iodide, *Iodoethane*, C_2H_5I, m.p. − 113°, b.p. 72°, $D_0 = 1{\cdot}975$, was discovered by Gay-Lussac in 1815. It is prepared from alcohol, iodine and phosphorus; or from diethyl sulphate with potassium iodide solution (C. 1906, II. 1589). It is a colourless, strongly refracting liquid.

Propyl iodide, C_3H_7I, b.p. 102°, D_{20} 1·7427, from propyl alcohol.

*iso***Propyl iodide,** C_3H_7I, b.p. 89·5°, $D_{20} = 1·7033$, is prepared from *iso*propyl alcohol, propylene glycol, $C_3H_6(OH)_2$, or from propylene, and, most conveniently, by distilling a mixture of glycerol, amorphous phosphorus, and iodine (Ann. **138**, 364):

$$C_3H_5(OH)_3 + 5HI = C_3H_7I + 2I_2 + 3H_2O.$$

Here allyl iodide, $CH_2{=}CH{-}CH_2I$, is first produced (see below), which is further changed to propylene, $CH_2{=}CH{-}CH_3$, and *iso*propyl iodide.

Amyl halides, see Ann. **385**, 274.

II. HALOGEN ESTERS OF THE UNSATURATED ALCOHOLS

The most important unsaturated halides are the **allyl halides** and the **propargyl halides.** The former are prepared from allyl alcohol by methods similar to those employed for the preparation of the corresponding compounds from ethyl alcohol. They are isomeric with the β- and α-halogeno-propylenes (p. 124), from which they are distinguished by their adaptability for double decompositions:

	Formula.	Boiling Point.	Sp. Gravity.
Allyl fluoride	$CH_2{=}CH{\cdot}CH_2F$	— 10°	. . .
Allyl chloride	$CH_2{=}CH{\cdot}CH_2Cl$	46°	0·9379 (20°)
Allyl bromide	$CH_2{=}CH{\cdot}CH_2Br$	71°	1·461 (0°)
Allyl iodide	$CH_2{=}CH{\cdot}CH_2I$	101°	1·789 (16°)

The allyl halides are liquids with leek-like odour. Allyl chloride, heated to 100° with HCl, yields propylene chloride, $CH_2CHCl{\cdot}CH_2Cl$. Allyl bromide, heated to 100° with HBr, passes into trimethylene bromide, $CH_2Br{\cdot}CH_2{\cdot}CH_2Br$. The addition of halogens produces glycerol trihaloid esters.

Allyl iodide.—This is readily prepared from glycerol by the action of HI, or iodine and phosphorus. It may be supposed that at first $CH_2I{\cdot}CHI{\cdot}CH_2I$ forms, but is subsequently decomposed into allyl iodide and iodine. (Preparation: Ann. **185**, 191: **226**, 206.) With excess of HI or phosphorus iodide, allyl iodide is further converted into propylene and *iso*propyl iodide (see above).

By continued shaking of allyl iodide in alcoholic solution with mercury, C_3H_5HgI separates in colourless leaflets (see mercury ethyl). Iodine liberates pure allyl iodide from this:

$$C_3H_5HgI + I_2 = C_3H_5I + HgI_2.$$

Alcoholic potassium hydroxide converts allyl iodide into allyl ethyl ether. With potassium sulphide it yields *allyl sulphide* (p. 173); with potassium thiocyanate, *allyl thiocyanate,* which passes readily into allyl mustard oil (*q.v.*). Allyl iodide has also been used in the synthesis of unsaturated alcohols.

Name.	Formula.	Boiling Point.	Sp. Gravity.
Propargyl chloride (Ber. **8**, 398)	$CH{\equiv}C{\cdot}CH_2Cl$	65°	1·0454 (5°)
Propargyl bromide (Ber. **7**, 761)	$CH{\equiv}C{\cdot}CH_2Br$	89°	1·5200 (20°)
Propargyl iodide (Ber. **17**, 1132)	$CH{\equiv}C{\cdot}CH_2I$	115°	2·0177 (0°)

Propargyl chloride is produced when phosphorus trichloride acts on propargyl alcohol.

B. ESTERS OF NITRIC ACID

These are prepared by the interaction of alcohols and nitric acid (C. 1903, II. 338). Nitrous acid is always produced, as a consequence of secondary reactions oxidizing and may be destroyed by the addition of urea :

$$CO(NH_2)_2 + 2HNO_2 = CO_2 + 2N_2 + 3H_2O.$$

When much nitrous acid is present, it induces the decomposition of the nitric acid ester, and causes explosions.

Methyl nitrate, b.p. 60° ; $D_{20} = 1{\cdot}182$. When struck or heated to 150° it explodes very violently.

Ethyl nitrate, $C_2H_5{\cdot}O{\cdot}NO_2$, b.p. 86° ; $D_{15} = 1{\cdot}112$, is a colourless, pleasant-smelling liquid. It is almost insoluble in water, and burns with a white light. It will explode if suddenly exposed to a high temperature. Heated with ammonia, it passes into ethylamine nitrate. Tin and hydrochloric acid convert it into hydroxylamine.

By the action of hydroxylamine on ethyl nitrate in the presence of sodium ethoxide, the sodium salt of nitrohydroxamic acid is obtained. (Angeli)

$$EtONO_2 + NH_2OH \longrightarrow EtOH + HOON:NOH.$$

Ethyl nitrate is much used for the purpose of introducing nitro groups into compounds containing a reactive methylene group.

Propyl nitrate, $C_3H_7O{\cdot}NO_2$ (Ber. **14**, 421), b.p. 110° ; iso*propyl nitrate*, b.p. 101–102° ; iso*butyl nitrate*, b.p. 123° ; iso*amyl nitrate*, b.p. 148° ; n-*octyl nitrate*, b.p. 110°/20 mm. ; *myristyl nitrate*, b.p. 175–180°/12 mm.

C. ESTERS OF NITROUS ACID

These are isomeric with the nitro-paraffins. The group NO_2 is present in both ; whilst, however, in the nitro-compounds nitrogen is combined with carbon, in the esters the union is effected by oxygen :

$C_2H_5{\cdot}NO_2$	$C_2H_5{\cdot}O{\cdot}NO.$
Nitro-ethane.	Ethyl nitrite.

The nitrous esters, as might be inferred from their different structure, decompose into alcohols and nitrous acid when acted on by alkalis. Similar treatment will not decompose the nitro-compounds. Nascent hydrogen (tin and hydrochloric acid) converts the latter into amines, whilst the esters are hydrolysed.

Esters of nitrous acid are produced in (1) the action of nitrous acid on the alcohols in dilute aqueous solution (Ber. **34**, 755) ; (2) by the action of alkyl iodides on silver nitrite (Ber. **25**, R. 571) nitro-paraffins of much higher boiling point being simultaneously produced, (3) by the introduction of nitrosyl chloride into a pyridine solution of the alcohol (C. 1903, II. 339).

Methyl nitrite, $CH_3{\cdot}O{\cdot}NO$, b.p. − 12°.

Ethyl nitrite, $C_2H_5{\cdot}O{\cdot}NO$, b.p. 16°, $D_{15} = 0{\cdot}947$, is obtained by the action of sulphuric acid and potassium nitrite on alcohol (Ann. **253**, 251, footnote). It is a mobile, yellowish liquid. It is insoluble in water, and possesses an odour resembling that of apples. It is the active ingredient of *spiritus ætheris nitrosi.*

When ethyl nitrite stands in contact with water it gradually decomposes, nitrogen oxide being evolved ; an explosion may occur under some conditions. Hydrogen sulphide changes it into alcohol and ammonia.

n-**Butyl nitrite,** $C_4H_9{\cdot}O{\cdot}NO$, b.p. 75°, *sec.*-**butyl nitrite,** b.p. 68°, *tert.*-**butyl nitrite,** b.p. 77°.

*iso***Amyl nitrite,** $C_5H_{11}O{\cdot}NO$, b.p. 96° ; $D = 0{\cdot}902$, is obtained by passing nitrous fumes into amyl alcohol at 100°. It is a yellow liquid. An explosion takes place when the vapours are heated to 250°. Nascent hydrogen changes it into amyl alcohol and ammonia. Heated with methyl alcohol, it is transformed into methyl nitrite and amyl alcohol ; ethyl alcohol behaves analogously (Ber. **20**, 656).

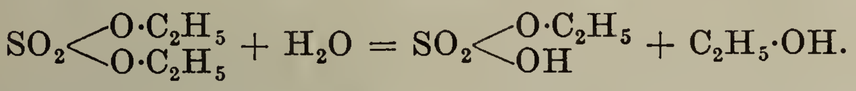
Amyl nitrite, "*Amylium nitrosum*," is used in medicine, and also for the preparation of nitroso- and diazo-compounds.

n-**Octyl nitrite**, b.p. 175° (C. 1903, II. 339).

NOTE.—Diazoethoxan, $C_2H_5O-N=N-OC_2H_5$, results from the interaction of iodoethane and nitrosyl silver $(NOAg)_2$. It is the ester of hyponitrous acid (Ber. **11**, 1630).

D. ESTERS OF SULPHURIC ACID

1. The normal, or **dialkyl esters** are prepared (1) by the interaction of alkyl iodides and silver sulphate; (2) from chlorosulphonic esters or sulphuryl chloride and sodium alcoholate, together with by-products (C. 1903, II. 936). They result (3), in small quantities, by heating ethyl hydrogen sulphate alone, or the alcohol with sulphuric acid, and can be extracted from the reaction products by chloroform. A better method is to pass methyl ether into H_2SO_4 at 160° (C. 1901, II. 269). Fuming sulphuric acid at ordinary temperatures yields mainly neutral esters with methyl and ethyl alcohols (C. 1900, II. 614). They are heavy liquids, soluble in ether, possess an odour like that of peppermint, and boil without decomposition. They will sink in water, and gradually decompose into a primary ester and alcohol:



$$SO_2{<}\begin{matrix}O\cdot C_2H_5\\ O\cdot C_2H_5\end{matrix} + H_2O = SO_2{<}\begin{matrix}O\cdot C_2H_5\\ OH\end{matrix} + C_2H_5\cdot OH.$$

Dimethyl sulphate, $SO_2(OCH_3)_2$, b.p. 188°, is conveniently prepared by the interaction of methyl alcohol and chlorosulphonic acid. It is highly irritating to the mucous membrane (C. 1901, I. 265), and is poisonous (C. 1902, I. 364). It is frequently employed in the preparation of methyl ethers, esters, and amines (Ann. **327**, 104).

Diethyl sulphate, $SO_2(OC_2H_5)_2$, b.p. 208°, may also be prepared from SO_3 and $(C_2H_5)_2O$. Heated with alcohol it forms ethyl sulphuric acid and ethyl ether (Ber. **13**, 1699; **15**, 947); it is an excellent reagent for alkylation (Ber. **33**, 2476) (comp. Ethyl hydrogen peroxide, p. 158).

Di-*iso*butyl sulphate, b.p. 134°/12 mm., and **Di-*iso*amyl sulphate**, b.p. 150°/12 mm., are prepared from the sodium derivatives of the corresponding alcohol and sulphuryl chloride (C. 1903, II. 937).

2. The **alkyl hydrogen esters** or *acid esters* are produced (1) when the alcohols are mixed with concentrated sulphuric acid:

$$SO_3(OH)_2 + C_2H_5\cdot OH = HO\cdot SO_2\cdot OC_2H_5 + H_2O.$$

The reaction takes place only when aided by heat, and it is not complete. The reaction proceeds to completion if the alcohol be dissolved in very little sulphuric acid, and SO_3 in the form of fuming sulphuric acid be then allowed to act on the well-cooled solution (Ber. **28**, R. 31). To isolate the acid esters, the product of the reaction is diluted with water and boiled with an excess of barium carbonate. In this way the unaffected sulphuric acid is thrown out as barium sulphate; the barium salts of the acid esters are soluble and crystallize out when the solution is evaporated. To obtain the acids in a free state their salts are treated with sulphuric acid or the lead salts (obtained by saturating the acids with lead carbonate) may be decomposed by hydrogen sulphide, and the solution allowed to evaporate over sulphuric acid.

Secondary alcohols, also, by careful cooling of the reacting bodies, are capable of forming acid esters—*e.g.* ethylpropylcarbinol (Ber. **26**, 1203); tertiary alcohols behave similarly (C. 1897, II. 408).

(2) The alkyl hydrogen esters also result from the union of the alkylenes with concentrated sulphuric acid.

Properties.—These esters are thick liquids, which cannot be distilled, but which sometimes crystallize. They dissolve readily in water and alcohol, but are insoluble in ether.

(1) When boiled or warmed with water they break down into sulphuric acid and alcohol:

$$HO{\cdot}SO_2{\cdot}C_2H_5 + H_2O = H_2SO_4 + C_2H_5{\cdot}OH.$$

(2) When distilled, they yield sulphuric acid and alkylenes (p. 102).

(3) When heated with alcohols, simple and mixed ethers (p. 154) are produced.

They show a strongly acid reaction, and furnish salts which dissolve readily in water, most of which crystallize readily. The salts gradually change to sulphates and alcohol when they are boiled with water. The alkali salts are frequently applied in synthetic reactions. Thus with KSH and K_2S they yield mercaptans and thio-ethers (p. 170); with salts of fatty acids they furnish esters, and with KCN the alkyl cyanides, etc.

Compounds of the type $R{\cdot}OSO_3H$ occur naturally in the urine, where they form the fraction described usually as "ethereal sulphate": they form one method by which the body detoxicates phenols, ingested or produced in metabolism.

Methyl hydrogen sulphate, $SO_4(CH_3)H$, is a thick oil.

Ethyl hydrogen sulphate, $SO_4(C_2H_5)H$, is obtained by mixing 1 part alcohol with 2 parts concentrated sulphuric acid: *potassium salt*, $SO_4(C_2H_5)K$, is anhydrous, and crystallizes in plates: *barium* and *calcium* salts crystallize in large tablets with two molecules of H_2O each (Ann. **218**, 300).

The *chlorides* or *chloroanhydrides* of the alkyl sulphuric acids ($Cl{\cdot}SO_2{\cdot}OR$), called **chlorosulphonic esters,** result (1) by the action of sulphuryl chloride on the alcohols (C. 1903, II. 936: 1905, I. 14):

$$C_2H_5{\cdot}OH + SO_2Cl_2 = \underset{\substack{\text{Chloride of ethyl}\\ \text{sulphuric acid.}}}{Cl{\cdot}SO_2{\cdot}OC_2H_5} + HCl;$$

(2) by the action of PCl_5 on salts of the ester acids; (3) by the union of the olefines with $Cl{\cdot}SO_3H$; (4) by the union of SO_3 with the alkyl chlorides; and (5) by the action of SO_2 on the esters of hypochlorous acid (Ber. **19**, 860):

$$SO_2 + ClO{\cdot}C_2H_5 = Cl{\cdot}SO_2{\cdot}OC_2H_5.$$

They are liquids possessing a penetrating odour. Cold water decomposes them slowly into the alkyl sulphuric acids. The same result accompanied by a violent evolution of ethyl chloride is brought about by alcohol. Sodium alcoholates and chlorosulphonic esters unite to form compounds which break down, giving rise to normal sulphonic ester, ether, sodium alkyl sulphate, and sodium sulphate. Aniline and phenols (Vol. II) are alkylated by chlorosulphonic ester; sodium malonic ester and sodium acetic ester are chlorinated (C. 1905, I. 13).

Ethyl chlorosulphonate, $C_2H_5{\cdot}O{\cdot}SO_2Cl$, b.p. 52°/14 mm.; $D_{18} = 1{\cdot}263$: *methyl ester*, $CH_3{\cdot}O{\cdot}SO_2Cl$, b.p. 132°.

E. ESTERS OF SULPHUROUS ACID

The empirical formula of sulphurous acid, H_2SO_3, may have two possible structures:

$$\underset{\text{(I)}}{HO{\cdot}SO{\cdot}OH} \qquad \text{or} \qquad \underset{\text{(II)}}{H{\cdot}SO_2{\cdot}OH}$$

The ordinary sulphites correspond with formula (II), and it appears that in them one atom of metal is in direct combination with sulphur:

$$\underset{\text{Silver sulphite.}}{Ag{\cdot}SO_2{\cdot}OAg} \qquad\qquad \underset{\text{Prim. potassium sulphite.}}{K{\cdot}SO_2{\cdot}OH}$$

Silver sulphite, $AgSO_2 \cdot OAg$, when acted on by iodoethane, yields the ethyl ester of ethanesulphonic acid, $C_2H_5 \cdot SO_3 \cdot C_2H_5$, which loses an ethyl group when treated with potassium hydroxide, and yields ethanesulphonic acid, $C_2H_5 \cdot SO_3H$, the oxidation product of ethyl mercaptan, C_2H_5SH. The *sulphonic acids* and their esters, which must be viewed as esters of unsymmetrical sulphurous acid, will be described after the mercaptans.

The esters of symmetrical and unsymmetrical sulphurous acid are closely connected, as the following shows.

If SO_2 is passed into a solution of sodium or potassium alcoholate, or SO_2 and NH_3 into absolute alcohol, there are obtained unstable salts of alkyl sulphurous acids—$CH_3O \cdot SO_2Na$, $C_2H_5O \cdot SO_2K$, $C_3H_7O \cdot SO_2Na$, $C_2H_5O \cdot SO_2NH_3$, which easily lose SO_2 (Ber. **38**, 1298 : C. 1902, II. 930). These salts are isomeric with the very stable alkyl sulphonic acid esters (p. 175). If *sodium ethyl sulphite* is heated with iodoethane or sodium iodide in alcoholic solution, it is converted into the double salt of *sodium ethanesulphonate* with sodium iodide.

The dialkyl esters of symmetrical sulphurous acid are prepared by the action of thionyl chloride $SOCl_2$ or sulphur chloride on the alcohols :

$$SOCl_2 + 2C_2H_5OH = SO(OC_2H_5)_2 + 2HCl.$$

$$S_2Cl_2 + 3C_2H_5OH = SO(OC_2H_5) + C_2H_5SH + 2HCl.$$

The mercaptan which is formed undergoes further change.

The dialkyl sulphites are liquids, insoluble in water, having an odour of peppermint. They are isomeric with the corresponding esters of the alkyl sulphonic acids. It is remarkable that aqueous solutions of alkali hydroxides only hydrolyse the sulphites with difficulty, whilst the prolonged action of a cold concentrated solution partially converts them into alkyl sulphonic acids ; a change which is also brought about by potassium iodide (see above) (Ber. **38**, 1298).

Dimethyl sulphite, $SO(O \cdot CH_3)_2$, b.p. 121° ; *diethyl sulphite*, b.p. 161° ; *dipropyl sulphite*, b.p. 191°.

Chlorosulphinic esters, $Cl \cdot SOOR$. The chlorosulphinic esters, which are obtained by the interaction of equimolecular quantities of thionyl chloride and alcohols in the cold, are derivatives of the hypothetical alkyl hydrogen sulphites.

$$SOCl_2 + R \cdot OH \longrightarrow Cl \cdot SO \cdot OR + HCl.$$

They are liquids, easily decomposed by water into hydrochloric acid, sulphur dioxide and the alcohol. By distillation under ordinary pressure they are partly decomposed into sulphur dioxide and the alkyl chloride (Ber. **44**, 319).

Methyl chlorosulphinate, b.p. 102° : *ethyl* ester, b.p. 122°. The ethyl ester is also obtained by the action of PCl_3 or thionyl chloride on diethyl sulphite.

F. ESTERS OF HYPOCHLOROUS AND PERCHLORIC ACIDS

The esters of hypochlorous acid are formed by mixing the free acid with the alcohols (Ber. **18**, 1767 : **19**, 857) or more conveniently from the alcohol, sodium hydroxide and chlorine (J.C.S. **123**, 2999). They are pungent-smelling, explosive liquids, which under suitable conditions break down quantitatively into HCl and an aldehyde or ketone (see p. 225).

Methyl hypochlorite, $CH_3 \cdot OCl$, b.p. 12° : *ethyl* ester, b.p. 36°.

The esters of perchloric acid are obtained from silver perchlorate and alkyl iodides.

G. ESTERS OF OTHER INORGANIC OXY-ACIDS

These esters are obtained by the action of BCl_3, B_2O_3, $POCl_3$, PCl_3, $AsBr_3$, $SiCl_4$, Si_2OCl_6 on alcohols and sodium alcoholates. Alkali hydroxides hydrolyse them with the production of alcohols and alkali salts of the respective inorganic acids. Most of them are decomposed entirely or in part by water.

Boric acid.—*Methyl borate,* $B(OCH_3)_3$, b.p. 65°, and *ethyl borate,* $B(OC_2H_5)_3$, b.p. 119°, both burn with a green flame (C. 1898, II. 1243).

Metaphosphoric acid.—The esters $R{\cdot}O{\cdot}PO_2$ are obtained from silver metaphosphate and alkyl iodides, or from ethers and phosphorus pentoxide. They are thick syrups, which cannot be distilled *in vacuo* without decomposition, and which unite with water or alcohols with formation of mono- and di-alkyl esters of orthophosphoric acid (Ber. **44**, 2076).

Orthophosphoric acid.—*Triethyl ester,* $PO(OFt)_3$, b.p. 211° (C. 1900, I. 102). Mono-esters of phosphoric acid, see Compt. rend. **168**, 560.

Thiophosphoric acid.—The esters $PS(OR)_3$ are obtained from thiophosphoryl chloride, $PSCl_3$, and sodium alcoholates. *Methyl ester,* b.p. 82°/20 mm.; *ethyl ester,* b.p. 106°/20 mm. (see J.C.S. **99**, 713; J. pr. Chem. [2] **84**, 746: Ber. **58**, 840).

Phosphorous acid.—The symmetrical esters, $P(OR)_3$, are obtained from phosphorus trichloride and the sodium alcoholates, and are converted by water or dilute acids into the dialkyl esters, $POH(OR)_2$, which are also obtained by the action of phosphorus trichloride on the alcohols. *Methyl ester,* b.p. 111°; *ethyl ester,* b.p. 156°. The symmetrical esters are isomerized by alkyl iodides into the alkylphosphonic esters (see p. 208) with intermediate formation of an addition compound:

$$HPO(OR)_2 \longleftarrow P(OR)_3 \longrightarrow RPO(OR)_2.$$

The symmetrical esters also form addition compounds with the cuprous halides (C. 1903, II. 22: 1906, II. 1639: 1914, I. 2156: Ber. **38**, 1171: **45**, 298).

Arsenic acid.—The *ethyl ester,* $AsO(OEt)_3$, b.p. 235°, is obtained from silver arsenate and ethyl iodide.

Arsenious acid.—The symmetrical *triethyl ester,* $As(OEt)_3$, b.p. 166°, is obtained by heating arsenious oxide with alcohol in presence of anhydrous copper sulphate (C. 1908, II. 849). The symmetrical derivatives of **antimonious acid,** $Sb(OR)_3$, are obtained similarly (C. 1909, I. 1976).

Vanadic acid.—Esters, see C. 1913, II. 1029.

Phosphonic and phosphinic acids and the corresponding compounds of arsenic, are described after phosphorus bases and arsenic bases.

Silicates.—*Methyl orthosilicate,* $Si(OCH_3)_4$, b.p. 120–122°. *Ethyl orthosilicate,* $Si(OC_2H_5)_4)$, b.p. 165°. *Ethyl disilicate,* $Si_2O(OC_2H_5)_6$, b.p. 236°. *Ethyl metasilicate,* $SiO(OC_2H_5)_2$, b.p. 360° (approximately).

The silicic esters burn with a brilliant white flame. The ortho- and metasilicic esters correspond with the ortho- and ordinary carbonic acid esters: $C(OC_2H_5)_4$ and $CO(OC_2H_5)_2$.

The orthoformic esters $HC(OR)_3$ correspond with the orthosilicoformic esters, $HSi(OR)_3$, which are produced from silicochloroform, $SiHCl_3$, and the alcohols. Ethyl orthosilicoformate, $HSi(OC_2H_5)_3$, b.p. 134°; *propyl orthosilicoformate,* b.p. 192°, D = 0·885. These esters yield silicon hydride when heated with sodium (Ber. **38**, 1661).

3. SULPHUR DERIVATIVES OF THE ALCOHOL RADICALS

The hydrosulphides and sulphides correspond with the metallic hydroxides and oxides, whilst the sulphur analogues of the alcohols and ethers are the *mercaptans* and *alkyl-sulphides,* and the alkali polysulphides find their analogues in the *alkyl polysulphides*:

$Na{\cdot}SH$	Na_2S	Na_2S_2
$C_2H_5{\cdot}SH$	$(C_2H_5)_2S$	$(C_2H_5)_2S_2$
Ethyl mercaptan.	Ethyl sulphide.	Ethyl disulphide.

I. MERCAPTANS, THIO-ALCOHOLS, OR ALKYL HYDROSULPHIDES

Although the mercaptans closely resemble the alcohols in general, they are differentiated in that the hydrogen, which in the alcohols is replaceable by the alkali metals, is in the mercaptans also to be substituted by the heavy metals. The mercaptans react very readily with mercuric oxide, to form crystalline compounds :

$$2C_2H_5{\cdot}SH + HgO = (C_2H_5{\cdot}S)_2Hg + H_2O.$$

Hence their designation as mercaptans (from *mercurium captans*). The metal derivatives of the mercaptans are termed *mercaptides*.

Formation.—(1) By the action of the alkyl halides on potassium hydrosulphide in alcoholic solution :

$$C_2H_5Cl + KSH = C_2H_5{\cdot}SH + KCl.$$

A modification of this method consists in allowing alcohols to react with bromine and red phosphorus in the presence of sodium sulphate, when the first-formed alkyl bromide yields mercaptans by reaction with the NaSH formed by the reducing action of the phosphorous acid (Chem. Abstr. 9, 1899).

(2) By distilling salts of the sulphuric esters with potassium hydrosulphide or potassium sulphide (see p. 168) :

$$KO{\cdot}SO_2{\cdot}OC_2H_5 + KSH = C_2H_5{\cdot}SH + K_2SO_4.$$

The neutral esters of sulphuric acid—*e.g.* $SO_2(O{\cdot}C_2H_5)_2$ (p. 167)—also yield mercaptans when heated with KSH.

(3) A direct replacement of the oxygen of alcohols and ethers by sulphur may be effected by phosphorous pentasulphide :

$$5C_2H_5OH + P_2S_5 = 5C_2H_5{\cdot}SH + P_2O_5.$$

(4) By reduction of the chlorides of the sulphonic acids (*q.v.*) :

$$C_2H_5{\cdot}SO_2Cl + 6H = C_2H_5SH + HCl + 2H_2O.$$

This reaction recalls the reduction of the acid chlorides to primary alcohols.

(5) By leading a mixture of alcohol vapour and H_2S over thoria at 300–360° (Compt. rend. **156,** 1217 : J.A.C.S. **43,** 880).

Properties and Reactions.—The mercaptans are colourless liquids, mostly insoluble in water, and possess a disagreeable, garlic-like odour.

(1) Moderate oxidation with concentrated sulphuric acid, sulphuryl chloride, or iodine converts the mercaptans or mercaptides into disulphides (p. 173). The reaction permits of these substances being titrated with iodine (Ber. **39,** 738).

(2) When oxidized with nitric acid, the mercaptans yield the sulphonic acids. Conversely, the mercaptans result by the reduction of the sulphonic acids.

(3) By their union with aldehydes and ketones there result *mercaptals* and *mercaptoles*—*e.g.* $CH_3CH(SC_2H_5)_2$, $(CH_3)_2C(SC_2H_5)_2$—which will be treated at the conclusion of the aldehydes and ketones (*q.v.*).

(4) The mercaptans unite more or less easily to an ethylene linkage, forming sulphides (Ber. **38,** 646).

Ethyl mercaptan, $C_2H_5{\cdot}SH$, b.p. 36° ; $D_{20} = 0{\cdot}829$. It is the most important and was the first-discovered mercaptan (1834, *Zeise*, Ann. **11,** 1). Despite its revolting odour, it is technically made from ethyl chloride and potassium sulphydrate in the preparation of *sulphonal.* It is but slightly soluble in water ; readily in alcohol and ether.

Mercury mercaptide, $(C_2H_5{\cdot}S)_2Hg$, m.p. 86°, crystallizes from alcohol in brilliant leaflets, and is only slightly soluble in water. When mercaptan is mixed with an alcoholic solution of $HgCl_2$, the compound $C_2H_5{\cdot}S{\cdot}HgCl$ is precipitated. The potassium and sodium compounds are best obtained by dissolving the metals in mercaptan diluted with ether; they crystallize in white needles.

Methyl mercaptan	b.p. 6°;	n-*butyl mercaptan*	b.p. 98°;
n-*propyl mercaptan*	b.p. 68°;	*allyl mercaptan*	b.p. 90°.
iso*propyl mercaptan*	b.p. 59°;		

Methyl mercaptan is formed during the fermentation of proteins (Ber. **34**, 201). n-*Butyl mercaptan* is found in secretions of the stink-badger of the Philippines (*Mydäus marchei huet*) (Pharm. Centralhalle, 1896, No. 34).

II. SULPHIDES OR THIO-ETHERS

These are obtained like the mercaptans:

(1) By the action of alkyl halides on potassium sulphide.

$$2C_2H_5Cl + K_2S = (C_2H_5)_2S + 2KCl.$$

(2) By distillation of salts of the alkylsulphuric acids with potassium sulphide:

$$2KO{\cdot}SO_2{\cdot}OC_2H_5 + K_2S = (C_2H_5)_2S + 2K_2SO_4.$$

(3) By the action of P_2S_5 on ethers:

$$5(C_2H_5)_2O + P_2S_5 = 5(C_2H_5)_2S + P_2O_5.$$

(4) On heating the lead mercaptides:

$$(C_2H_5S)_2Pb = (C_2H_5)_2S + PbS.$$

(5) By the interaction of alkyl halides with potassium or sodium mercaptides, when mixed thio-ethers can be produced:

$$C_2H_5SNa + C_2H_5I = (C_2H_5)_2S + NaI$$
$$C_2H_5SNa + C_3H_7I = C_2H_5{\cdot}S{\cdot}C_3H_7 + NaI.$$

(6) By passing mercaptan vapours over cadmium sulphide at 320–330° (Compt. rend. **150**, 1569).

Methods 1, 2, 5 and 6 are analogous to those used in the preparation of the corresponding ethers.

The sulphides, like the mercaptans, are colourless liquids, insoluble in water, but easily soluble in alcohol and ether. When impure, their odour is very disagreeable, but is ethereal when pure (Ber. **27**, 1239).

Reactions.—The sulphides are characterized by their additive power. (1) They unite with Br_2, and (2) with metallic salts—*e.g.* $(C_2H_5)_2S,HgCl_2$, $[(C_2H_5)_2S]_2,PtCl_4$ (C. 1900, I. 280: 1901, II. 184): (3) also with alkyl iodides to form sulphonium iodides (p. 173); (4) they are oxidized to sulphoxides (p. 174) and sulphones (p. 174) by nitric acid.

Methyl sulphide, $(CH_3)_2S$, b.p. 37·5°; *ethyl sulphide,* $(C_2H_5)_2S$, b.p. 91°; n-*propyl sulphide,* $(C_3H_7)_2S$, b.p. 130–135°; n-*butyl sulphide,* b.p. 182°; iso*butyl sulphide,* $[(CH_3)_2CH{\cdot}CH_2]_2S$, b.p. 173°; *cetyl sulphide,* $(C_{16}H_{33})_2S$, m.p. 57°.

Dichloromethyl sulphide, b.p. 156°, is obtained from trithioformaldehyde and S_2Cl_2 (Ber. **55**, 53).

ββ′-Dichlorodiethyl sulphide, $(ClCH_2{\cdot}CH_2)_2S$, m.p. 13–13·5°, b.p. 215–217° (dec.), was used as mustard-gas (Ger. *Gelbkreuz*) during the war. It was prepared in two ways:

(1) From ethylene chlorohydrin and Na_2S, the thiodiglycol $(HOCH_2CH_2)S$ thus formed being converted into the dichloro derivative by heating with concentrated HCl (J.A.C.S. **41**, 1414).

(2) From ethylene and SCl_2 or S_2Cl_2 (J.C.S. **117**, 271). Pharmacological action, see Zeitschr. f. d. ges. exp. Med. **13**, 367.

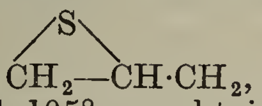
Unsaturated sulphides.—The sulphides of vinyl and allyl alcohols occur in nature. They are far more important than the sulphides of the normal alcohols, particularly allyl sulphide.

Vinyl sulphide $(C_2H_3)_2S$, b.p. 101°; D = 0·9125, is the principal ingredient of the oil of *Allium ursinum*, and is very similar to allyl sulphide. It forms $(C_2H_3Br_2)_2SBr_2$ with six atoms of bromine. Silver oxide changes it to vinyl ether (p. 158) (Ann. **241**, 90).

Allyl sulphide, $(C_3H_5)_2S$, b.p. 140°, may be prepared by digesting allyl iodide with potassium sulphide in alcoholic solution. It is a colourless, disagreeable-smelling oil, but slightly soluble in water. It forms crystalline precipitates with alcoholic solutions of $HgCl_2$ and $PtCl_4$. With silver nitrate it yields the crystalline compound $(C_3H_5)_2S,2AgNO_3$.

The early statement of Wertheim that allyl sulphide is to be found in garlic, has not been substantiated; it is the disulphide which occurs there (C. 1892, II. 833).

Allyl mustard oil is produced by heating the mercury derivative with potassium thiocyanate. Vinyl mustard oil is prepared in an analogous manner.



$\alpha\beta$-**Propylene sulphide,** $CH_2—CH{\cdot}CH_2$ (with S bridging the first two carbons), and the corresponding $\alpha\beta$-**butylene** compound, b.pp. 77° and 104–105°, are obtained from the corresponding dibromides, through the dithiocyanates, by the action of Na_2S (Compt. rend. **172**, 158).

Alkyl disulphides are produced (1) like the alkyl monosulphides by distilling salts of the ethyl sulphuric acids or alkyl halides with potassium disulphide (C. 1901, I. 1363):

$$KO{\cdot}SO_2{\cdot}OC_2H_5 + K_2S_2 = (C_2H_5)_2S_2 + 2K_2SO_4.$$

(2) by the action of iodine on mercaptans, or concentrated sulphuric acid on mercaptides (Ber. **39**, 738). When bromine acts on a mixture of two mercaptans, mixed alkyl disulphides are produced (Ber. **19**, 3132):

$$2C_2H_5SH + I_2 = (C_2H_5)_2S_2 + 2HI.$$

(3) by the action of sulphuryl chloride on the mercaptans:

$$2C_2H_5SH + SO_2Cl_2 = (C_2H_5)_2S_2 + SO_2 + 2HCl.$$

Nascent hydrogen reduces the alkyl disulphides to mercaptans, whilst zinc dust converts them into zinc mercaptides:

$$(C_2H_5)_2S_2 + Zn = (C_2H_5S)_2Zn.$$

Mercaptides result on heating the disulphides with potassium sulphide (Ber. **19**, 3129); magnesium alkyl halides produce sulphides and mercaptides (C. 1906, I. 1244), and dilute nitric acid changes them to alkyl thiosulphonic esters (p. 177).

Methyl disulphide, $(C_2H_3)_2S_2$, b.p. 112°, and *ethyl disulphide,* $(C_2H_5)_2S_2$, b.p. 151°, are oils possessing an odour like that of garlic.

Allyl disulphide, $(C_3H_5)_2S_2$, b.p. 117°/16 mm., occurs with closely connected polysulphides in garlic, *Allium sativum* (C. 1892, II. 833). The name "allyl" is derived from this.

III. SULPHONIUM COMPOUNDS

(Ber. **27**, 505 Anm.)

(1) The sulphides of the alcohol radicals (thio-ethers) combine with the iodides, bromides, and chlorides of the alcohol radicals at ordinary temperatures, more rapidly on application of heat, and form crystalline *sulphonium* compounds:

$$(C_2H_5)_2S + C_2H_5I = \underset{\text{Triethyl sulphonium iodide.}}{(C_2H_5)_3\overset{IV}{S}I.}$$

These are perfectly analogous to the halogen derivatives of the strong basic radicals. By the action of moist silver oxide the halogen atom in them may be replaced by hydroxyl, and hydroxides similar to potassium hydroxide are formed :

$$(C_2H_5)_3SI + AgOH = (C_2H_5)_3S{\cdot}OH + AgI.$$

(2) The sulphine or sulphonium halides are also obtained on heating the alkyl sulphides with the halogen acids, or (3) with iodine (Ber. **25**, R. 641) :

$$2(C_2H_5)_2S + HI = (C_2H_5)_3SI + C_2H_5SH.$$
$$4(CH_3)_2S + I_2 = 2(CH_3)_3SI + (CH_3)_2S_2.$$

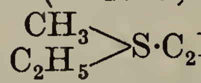
(4) The acid chlorides react similarly to iodine.

(5) By the action of iodomethane on metallic sulphides :

$$SnS + 3CH_3I = SnI_2 + (CH_3)_3SI.$$

By heating together sulphur and iodomethane to 180° there is formed $(CH_3)_3SI{\cdot}I_2$ an iodine addition product of trimethyl sulphonium iodide. Similar compounds are obtained with selenium and tellurium (C. 1904, II. 414).

Often when the alkyl iodides act on the higher alkyl sulphides the latter are displaced (Ber. **8**, 825).

$(C_2H_5)_2S{\cdot}CH_3I$ and  $\begin{matrix}CH_3\\C_2H_5\end{matrix}{>}S{\cdot}C_2H_5I$ are not isomeric (in which case a difference of the 4 valences of S would be proved) but identical (Ber. **22**, R. 648).

The sulphonium hydroxides are crystalline, efflorescent, strongly basic bodies, readily soluble in water. Like the alkalis, they precipitate metallic hydroxides from metallic salts, set ammonia free from ammoniacal salts, absorb CO_2 and saturate acids, with the formation of neutral salts :

$$(C_2H_5)_3S{\cdot}OH + HNO_3 = (C_2H_5)_3S{\cdot}NO_3 + H_2O.$$

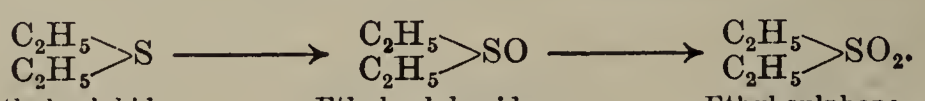
We thus observe that relations similar to those noted with the nitrogen group prevail with sulphur (also with selenium and tellurium). Nitrogen and phosphorus combine with four hydrogen atoms, also with alcoholic radicals, to form the groups ammonium, NH_4, and phosphonium, PH_4, which yield compounds similar to those of the alkali metals. Sulphur and its analogues combine in like manner with three univalent alkyls, and give sulphonium and sulphine derivatives. Other non-metals and the less positive metals, like lead and tin, exhibit a perfectly similar behaviour. By addition of hydrogen or alkyls they acquire a strongly basic, metallic character (see the metallo-organic compounds and also the aromatic iodonium bases, Vol. II).

Trimethyl sulphonium iodide, $(CH_3)_3SI$, is readily soluble in water, but is soluble with difficulty in alcohol, from which it crystallizes in white needles. At 215° it breaks down directly into methyl sulphide and iodomethane. Platinic chloride precipitates, from solutions of the chloride, a chloroplatinate, $[(CH_3)_3SCl]_2{\cdot}PtCl_4$, very similar to ammonium platinum chloride. *Trimethyl sulphonium hydroxide,* $(CH_3)_3SOH$, consists of deliquescent crystals possessing a strongly alkaline reaction.

Consult Ber. **24**, R. 906, for the refractive power and the lowering of the freezing point of sulphine compounds.

IV. SULPHOXIDES AND SULPHONES

These, as mentioned (p. 172), result from the oxidation of the sulphides :



$$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}{>}S \longrightarrow \begin{matrix}C_2H_5\\C_2H_5\end{matrix}{>}SO \longrightarrow \begin{matrix}C_2H_5\\C_2H_5\end{matrix}{>}SO_2.$$

Ethyl sulphide. Ethyl sulphoxide. Ethyl sulphone.

The **sulphoxides** are formed from the sulphides by oxidation by nitric acid or hydrogen peroxide (C. 1909, I. 350). The unsymmetrical sulphoxides, $R{\cdot}SO{\cdot}R'$, have been obtained in optically active forms, showing that the three groups attached to the sulphur atom are not co-planar (J.C.S. **1926**, 2079) (see p. 31). The sulphoxides are reduced to sulphides by nascent hydrogen.

Methyl and *ethyl sulphoxides* are thick oils, which combine with nitric acid to the compounds $R_2SO{\cdot}HNO_3$. The free sulphoxides are regenerated from these salts by barium carbonate. Methyl sulphoxide is also obtained from the bromide Me_2SBr_2 and silver oxide.

The **sulphones** are obtained from the sulphoxides by oxidation with fuming nitric acid or permanganate, or from the alkali salts of the alkylsulphinic acids and alkyl iodides :

$$R{\cdot}SO_2K + R'I \longrightarrow R{\cdot}SO_2{\cdot}R' + KI.$$

They are not, however, the true esters of the sulphinic acids, but are very stable compounds in which both alcohol radicals are linked to sulphur. They cannot be reduced to the sulphides.

Dimethyl sulphone, $(CH_3)_2SO_2$, m.p. 109° ; b.p. 238°.
Diethyl sulphone, $(C_2H_5)_2SO_2$, m.p. 70° ; b.p. 248°.

V. ALKYL SULPHONIC ACIDS, ALKYL THIOSULPHURIC ACIDS, ALKYL THIOSULPHONIC ACIDS, AND ALKYL SULPHINIC ACIDS

These compounds have the general formulæ :

$R{\cdot}SO_2OH$	$RS{\cdot}SO_3H$	$R{\cdot}SO_2SH$	$R{\cdot}SO_2H$
Sulphonic acid.	Thiosulphuric acid.	Thiosulphonic acid.	Sulphinic acid.

Sulphonic Acids

The sulphonic acids contain the sulpho-group—$SO_2{\cdot}OH$—joined to carbon. This is evident from their production by the oxidation of the mercaptans, and from their re-conversion into mercaptans (p. 171). They can be considered as being ester derivatives of the unsymmetrical sulphurous acid, HSO_2OH (p. 169).

Formation.—(1) Their salts result from the interaction of alkali sulphites and alkyl iodides ; their esters are formed when alkyl iodides act on silver sulphite :

$$K{\cdot}SO_2OK + C_2H_5I = C_2H_5{\cdot}SO_2OK + KI.$$

Potassium ethanesulphonate.

$$Ag{\cdot}SO_2OAg + 2C_2H_5I = C_2H_5{\cdot}SO_2OC_2H_5 + 2AgI.$$

Ethyl ethanesulphonate.

All the esters of sulphurous acid, both sulphites, $ROSO_2K$, and sulphonic esters, $(RO)_2SO$, when heated with KI form sulphonic acid double salts of the type $(RSO_3K)_4KI$.

(2) By oxidation of (*a*) the mercaptans ; (*b*) the alkyl disulphides ; (*c*) the alkyl thiocyanates with nitric acid :

$$\left.\begin{array}{r}C_2H_5SH\\ [C_2H_5S]_2\\ C_2H_5S{\cdot}CN\end{array}\right\} \xrightarrow{O} C_2H_5{\cdot}SO_3H.$$

(3) The alkyl sulphinic acids are readily oxidized to sulphonic acids.

(4) The sulphonic acids can be formed further by the action of sulphuric acid or sulphur trioxide on alcohols, ethers, and various other bodies. This reaction proceeds without difficulty in the aromatic series.

Properties and Reactions.—These acids are thick liquids, readily soluble in water, and generally crystallizable. They undergo decomposition when exposed to heat (Ber. **38**, 2019), but are not altered when boiled with alkali hydroxides. When fused with solid alkali hydroxides they break up into *sulphites* and alcohols :

$$C_2H_5{\cdot}SO_2{\cdot}OK + KOH = KSO_2{\cdot}OK + C_2H_5{\cdot}OH.$$

PCl_5 changes them to chlorides,—*e.g.* $C_2H_5{\cdot}SO_2Cl$,—which are reduced to mercaptans by hydrogen ; and by the action of sodium alcoholates they pass into the neutral esters—$C_2H_5{\cdot}SO_3{\cdot}C_2H_5$.

Many of these reactions plainly indicate that in the sulphonic acids the sulphur is directly combined with the alkyl groups. The sulphonic esters boil considerably higher than the esters of symmetrical sulphurous acid (p. 169). Whilst alcoholic potassium hydroxide converts the latter into potassium sulphite and alcohol, aqueous alkali solutions act only with difficulty and with the partial production of salts of alkyl sulphonic acids ; in the sulphonic esters the alkyl group which is not directly combined with sulphur is readily removed by hydrolysis.

Methanesulphonic acid, $CH_3{\cdot}SO_3H$, was synthetically prepared by Kolbe in 1845 from carbon disulphide, by converting it by means of moist chlorine into the chloride of trichloromethanesulphonic acid, CCl_3SO_2Cl, and this into the acid itself, which is reduced by sodium amalgam to methanesulphonic acid (Ann. **54**, 174) :

$$C + 2S = CS_2 \longrightarrow CCl_3{\cdot}SO_2Cl \longrightarrow CCl_3{\cdot}SO_3H \longrightarrow CH_3{\cdot}SO_3H.$$

Methanesulphonic chloride, CH_3SO_2Cl, b.p. 160° ; *ethyl ester,* b.p. 86°/10 mm. ; *anhydride,* $(CH_3SO_2)_2O$, m.p. 71°, b.p. 138°/10 mm. (Ber. **38**, 2018).

Chloroiodomethanesulphonic acid, $CHClI{\cdot}SO_3H$, is of interest as the first compound containing only one carbon atom to be resolved into its optically active components (Pope and Read, J.C.S. **105**, 811 : see also J.C.S. **1932**, 2723).

Ethanesulphonic acid, $C_2H_5{\cdot}SO_3H$, is oxidized by concentrated nitric acid to ethyl sulphuric acid, $C_2H_5O{\cdot}SO_3H$ (p. 168) ; *lead salt,* $(C_2H_5{\cdot}SO_3)_2Pb$, is readily soluble ; *methyl ester,* $C_2H_5SO_3CH_3$, b.p. 198° ; *ethyl ester,* $C_2H_5{\cdot}SO_3{\cdot}C_2H_5$, b.p. 213·4° ; *sulphochloride,* $C_2H_5{\cdot}SO_2Cl$, b.p. 177°.

Ethylenesulphonic acid, $CH_2{=}CHSO_3H$, is obtained from ethane disulphochloride, by the action of water and alcohol. Its *ammonium salt,* m.p. 156°, reduces alkaline permanganate instantaneously, and combines with ammonium hydrogen sulphite to form ammonium ethanedisulphonate (C. 1898, II. 1009 : 1899, I. 1104). *Ethylenesulphone anilide,* $CH_2 : CHSO_2NHC_6H_5$, and *propylenesulphone anilide,* $CH_3CH : CHSO_2NHC_6H_5$, are obtained from ethane- and propane-$\alpha\beta$-disulphonyl chlorides and aniline, with loss of SO_2 and HCl, even at 0° (Ber. **36**, 3626).

Alkyl Thiosulphuric Acids

The well-crystallized alkali salts of these acids are made by acting on alkali thiosulphates with primary saturated alkyl iodides (Ber. **7**, 646, 1157) or bromides (Ber. **26**, 996).

$$C_2H_5I + NaS{\cdot}SO_3Na = C_2H_5S{\cdot}SO_3Na + NaI.$$

Sodium ethyl thiosulphate is called *Bunte's salt,* after its discoverer. It also results when iodine acts on a mixture of sodium mercaptide and sodium sulphite :

$$C_2H_5SNa + NaSO_3Na + I_2 = C_2H_5S{\cdot}SO_3Na + 2NaI.$$

The free acids are not stable. Mineral acids convert sodium ethyl thiosulphate into mercaptan and mono-sodium sulphate. Heat breaks down the salts into disulphides, neutral potassium sulphate, and sulphur dioxide. Electrolysis of Bunte's salt gives rise to diethyl disulphide (C. 1901, I. 331).

Alkyl Thiosulphonic Acids

These acids are only stable as salts and esters. They are formed by the action of the chlorides of sulpho-acids on potassium sulphide:

$$C_2H_5{\cdot}SO_2Cl + K_2S = C_2H_5{\cdot}SO_2SK + KCl.$$

The *esters*, $R{\cdot}SO_2SR$, of this new class (formerly called alkyl disulphoxides, $R_2S_2O_2$) are obtained (1) from the alkali salts by the action of the alkyl bromides (Ber. **15**, 123):

$$C_2H_5{\cdot}SO_2{\cdot}SK + C_2H_5Br = C_2H_5{\cdot}SO_2{\cdot}SC_2H_5 + KBr;$$

and (2) by the oxidation of mercaptans and alkyl disulphides with dilute nitric acid: $(C_2H_5)_2S_2 + O_2 = C_2H_5{\cdot}SO_2{\cdot}SC_2H_5$. These esters are liquids, insoluble in water, and possessed of a disgusting odour (Ber. **19**, 1241, 3131). *Diethyl thiosulphate,* $C_2H_5{\cdot}SO_2{\cdot}S{\cdot}C_2H_5$, b.p. 130–140°.

Alkyl Sulphinic Acids

These acids can be considered as derived from the hypothetical sulphoxylic acid, H_2SO_2, by replacement of one hydrogen atom by an alkyl group. The existence of chlorides and anhydrides of the aromatic sulphinic acids (Ber. **41**, 3323, 4113) and the existence of the true sulphinic esters affords support for the formula $R{\cdot}SO{\cdot}OH$ as against the alternative $R{\cdot}SO_2{\cdot}H$.

The sulphinates are formed as follows:

(1) By the oxidation of the dry sodium mercaptides in air.

$$R{\cdot}SNa + O_2 \longrightarrow R{\cdot}SO_2Na$$

(2) By the action of SO_2 on zinc alkyls or magnesium alkyl halides or by the action of SO_2Cl_2 on the latter.

$$R_2Zn + SO_2 \longrightarrow (R{\cdot}SO_2)_2Zn$$
$$2RMgI + SO_2Cl_2 \longrightarrow R{\cdot}SO_2MgI + RCl + MgClI.$$

(3) By the action of zinc on the sulphonyl chlorides.

$$2R{\cdot}SO_2Cl + Zn \longrightarrow (R{\cdot}SO_2)_2Zn + ZnCl_2.$$

The sulphones (p. 175) are produced in the action of alkyl iodides on the alkali sulphinates, whilst the real esters result from the esterification of the acids with alcohol and hydrochloric acid, or by the action of chloroformic esters on the sulphinates (Ber. **18**, 2493):

$$R{\cdot}SO_2Na + Cl{\cdot}CO_2R = R{\cdot}SO{\cdot}OR + CO_2 + NaCl.$$

When these esters are hydrolysed by alcohol or water they break down into alcohol and sulphinic acid, whilst the isomeric sulphones are not altered. The free sulphinic acids are unstable liquids which dissolve in water and are oxidized to sulphonic acids. Potassium permanganate and acetic acid convert the sulphinic esters into sulphonic esters (Ber. **19**, 1225), whereas the isomeric sulphones remain unchanged.

4. SELENIUM AND TELLURIUM COMPOUNDS

These are very similar to the sulphur compounds.

Selenomercaptans.—*Ethyl selenomercaptan*, Et·SeH, b.p. 53·5°, is a colourless, foul-smelling liquid, immiscible with water, and readily oxidized. With mercuric oxide, it readily forms a mercaptide. n-*Propyl* and n-*butyl selenomercaptans* boil at 84° and 111°.

Selenides.—*Methyl ethyl selenide*, Me·Se·Et, b.p. 86°, from sodium ethylselenomercaptide and methyl iodide (Ber. **42**, 49). *Ethyl selenide*, b.p. 108°, is a heavy yellow oil which readily combines with halogens to compounds of the type Et_2SeCl_2. Nitric acid oxidizes it to the *selenoxide* Et_2SeO which forms the salt $Et_2Se(NO_3)_2$ with more nitric acid.

Selenites.—*Ethyl selenite*, $SeO(OEt)_2$, b.p. 184° (partial dec.), is obtained from selenyl chloride and sodium ethoxide, or from silver selenite and ethyl iodide. This is evidence in favour of the formula $SeO(OH)_2$ for selenious acid (Ann. **241**, 150).

Telluromercaptans are unknown.

Tellurides.—*Methyl* and *ethyl tellurides*, Me_2Te and Et_2Te, b.pp. 80–82° and 137·5°, are obtained as heavy yellow oils by distillation of barium alkyl sulphates with potassium telluride. Compounds of the following types are derived from the tellurides: R_2TeO, R_2TeCl_2, $R_2Te(NO_3)_2$, R_3TeI, R_3TeOH. The compound Me_2TeI_2, *dimethyltelluronium iodide*, exists in two isomeric forms. These were originally regarded as stereoisomers (J.C.S. **117**, 86, 889), but more recent work shows the isomerism to be structural (J.C.S. **1929**, 560).

Dimethyl tellurium oxide, $(CH_3)_2TeO$, is a crystalline efflorescent compound, resembling, in its basic properties, CaO and PbO. It reacts strongly alkaline, expels ammonia from ammonium salts, and neutralizes acids.

The compound Me_2TeO_2, *dimethyltellurone*, analogous to the sulphones, has also been prepared (J.C.S. **117**, 889).

The compound *phenyl-*p*-tolylmethyltelluronium iodide*, $C_6H_5(C_7H_7)TeMeI$, has been obtained in optically active forms (J.C.S. **1929**, 2867).

5. NITROGEN DERIVATIVES OF THE ALCOHOL RADICALS

A 1. MONONITRO-PARAFFINS AND -OLEFINES

By nitro-bodies are understood compounds of carbon in which the hydrogen combined with the latter is replaced by the univalent nitro-group, NO_2. The carbon is directly united to the nitrogen, as is shown by the reduction of the nitro-derivatives yielding amino-compounds:

$$R{\cdot}NO_2 + 6H = R{\cdot}NH_2 + 2H_2O.$$

In the aromatic series the hydrogen atoms of the benzene nucleus are readily replaced by nitro-groups, *e.g.*:

$$C_6H_6 + NO_2OH = \underset{\text{Nitrobenzene.}}{C_6H_5NO_2} + H_2O.$$

Comparative refractometric investigations have shown that the nitro-group in nitroethane, and that in nitrobenzene, do not have the same structure (Z. physik. Chem. **6**, 552). See Ber. **28**, R. 153, for the heat of combustion of the nitroparaffins.

(1) *Direct nitration.*—Normal paraffins are very stable towards nitric acid (p. 98), and are only acted on after prolonged heating at 130–140° with the dilute acid, whereby substitution products result (Konowalow, Ber. **26**, R. 108: **28**, 1863: C. 1898, I. 926: 1899, I. 966, 1063: 1902, I. 564: 1906, II. 312).

Experience shows that, amongst the fatty bodies, the hydrogen atom which is attached to a tertiary carbon atom is more easily replaced by the nitro-group than that which is attached to a secondary carbon atom, and this, in turn, more easily than one attached to a primary. Amongst secondary compounds, that hydrogen is the more easily replaced if its carbon atom is connected to a tertiary radical. *Markownikoff* has expressed this in the following rule: In hydrocarbons that hydrogen is always more easily replaced when attached to a carbon atom which is affected by other carbon atoms (Ber. **33**, 1907).

(2) A common method for the preparation of the nitroparaffins

consists in heating the iodides of the alcohol radicals with silver nitrite (*V. Meyer*, 1872) (Ann. **171**, 1 : **175**, 88 : **180**, 111) :

$$C_2H_5I + AgNO_2 = C_2H_5{\cdot}NO_2 + AgI.$$

The esters of nitrous acid, the alkyl nitrites, are formed simultaneously in this reaction (Ber. **15**, 1547). The silver nitrite behaves as if it consisted of $Ag{\cdot}NO_2$ and $Ag{\cdot}O{\cdot}NO$. Mercurous nitrite behaves similarly to the silver salt (Proc. Chem. Soc. **1907**, 246). Potassium nitrite, on the other hand, yields only the alkyl nitrite (*cf.* however, Method 3 (below) and C. 1907, I. 235). It is possible that the formation of the esters takes place through the intermediate formation of olefines, which then unite with the nitrous acid to form nitrites (Ann. **180**, 157 : Ber. **9**, 529) : more probably, an addition of the alkyl halide, either directly to the nitrogen atom, or with rupture of the N : O double bond takes place (J.C.S. **109**, 701).

(3) Simultaneously with the discovery of method 2, *Kolbe* demonstrated that nitromethane resulted from the action of potassium nitrite on chloroacetic acid. The first product in this instance was nitroacetic acid, which broke down into carbon dioxide and nitromethane (J. pr. Chem. [2] **5**, 427) :

$$CH_2Cl{\cdot}CO_2H \longrightarrow [CH_2(NO_2){\cdot}CO_2H] \longrightarrow CH_3NO_2 + CO_2.$$

By the same method α-bromopropionic acid and α-bromobutyric acid are made to yield nitroethane and nitropropane, and so on for the series (C. 1900, I. 126).

(4) The nitroparaffins are also formed by oxidation of the nitrosoparaffins (p. 183).

(5) Zinc alkyls, acting on chloro- and bromo-nitroparaffins, produce mononitroparaffins (Ber. **26**, 129) :

$$CH_3{\cdot}CHBrNO_2 \xrightarrow{Zn(CH_3)_2} CH_3{\cdot}CH(NO_2){\cdot}CH_3, \text{ Secondary nitropropane.}$$

$$CCl_3{\cdot}NO_2 \xrightarrow{Zn(CH_3)_2} C{\cdot}NO_2(CH_3)_3, \text{ Tertiary nitrobutane.}$$

Properties and Reactions.—The nitroparaffins are colourless, agreeably-smelling liquids, which are sparingly soluble in water. They distil without decomposition, and only explode with difficulty. Their boiling points lie considerably higher than those of the corresponding nitrous esters (p. 166: see also p. 32).

(1) *Action of alkalis.*—The action of potassium and sodium hydroxides on the nitroparaffins is to form salts when the NO_2 group stands next to a hydrogen atom in the molecule. Similar action on the isomeric nitrous esters results in the production of alcohol and an alkali nitrite.

Victor Meyer, who discovered the nitroparaffins and studied them closely, assumed that, in the salts, the alkali metal was united directly with the carbon atom (Ann. **171**, 28, 48) ; whilst *A. Michael* (J. pr. Chem. (1888), [2] **37**, 507) and later *Nef* (Ann. (1894), **280**, 263) showed it to be joined to an oxygen atom of the nitro-group.

Potassium-nitroethane, CH_3CHKNO_2 — According to V. Meyer. $CH_3{\cdot}CH{=}NOOK.$ — According to A. Michael.

The nitroparaffins are converted by alkalis into *iso*nitroparaffins (also called *aci*-nitroparaffins or nitronic acids), from which the salts are derived (compare p. 50). If a solution of such an alkali salt is acidified, the *iso*nitroparaffin which is first precipitated changes into the corresponding nitroparaffin. *A. F. Holleman* (compare Ber.

33, 2913) showed how this change could be followed by rapidly-taken conductivity measurements, since the labile, salt-forming *iso*nitro-body is an electrolyte, which turns into a stable, neutral, non-conducting nitro-compound. The rapidly falling conductivity runs parallel to the decolorization of the first-formed yellow solution. *Hantzsch* succeeded in isolating phenylnitromethane in both its forms—$C_6H_5CH_2NO_2$ and $C_6H_5CH:NOOH$ (Ber. **29**, 1223, 2251 : C. 1897, I. 1054).

A new formula for the *aci*-nitroparaffins, based on the octet theory, and which accounts for the persistence of the asymmetry in the alkali derivatives of *sec.*-nitrobutane, has been put forward by R. Kuhn, Ber. **60**, 1297.

By various methods, the *aci*-nitroparaffins can be converted into hydroxamic acids or their derivatives.

$$R{\cdot}CH:NO{\cdot}OH \longrightarrow R{\cdot}C{<}^{NOH}_{OH}$$

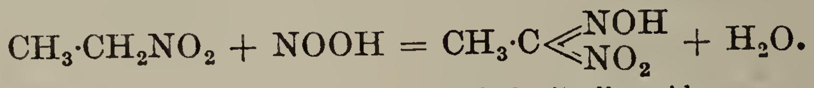
For example, the action of benzoyl chloride on sodium *aci*-nitroethane yields benzoylacethydroxamic acid, $CH_3C(OH):NO{\cdot}COC_6H_5$, instead of the expected benzoyl*aci*nitroethane (C. 1898, I. 564). By dropping a solution of an alkali salt of a primary nitroparaffin into ice-cold dilute hydrochloric acid, a small quantity is converted into the hydroxamic acid (Ber. **35**, 49). A number of primary nitro-compounds in ethereal solution are converted by gaseous HCl into hydroxamic chlorides (J. pr. Chem. [2] **84**, 686). The formation of hydroxylamine and a fatty acid by heating a primary nitro-compound with concentrated HCl is referable to a primary change into a hydroxamic acid (Ann. **180**, 163).

(2) *Reduction of nitroparaffins.*—By gradual reduction, the nitro-bodies (*V. Meyer*, Ber. **24**, 3528, 4243 : **25**, 1714) pass first into alkylhydroxylamines (p. 204) and then into primary amines :

$$\underset{\text{Nitromethane.}}{CH_3NO_2} \longrightarrow \underset{\text{N-Methylhydroxylamine.}}{CH_3{\cdot}NH{\cdot}OH} \longrightarrow \underset{\text{Methylamine.}}{CH_3NH_2.}$$

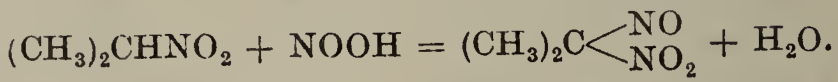
The conversion of nitroparaffins into primary amines proves, as indicated before, that the nitrogen of the nitro-group present in them is linked to carbon.

(3) *Reaction with nitrous acid.*—The varying behaviour of the nitroparaffins with nitrous acid at the moment of its formation from potassium nitrite and sulphuric acid is very interesting, according as the nitro-group is linked to primary, secondary, or tertiary radicals. **Primary nitro-compounds** in the presence of excess of potassium hydroxide give rise to an *intense red* colour due to a soluble, red-coloured alkali salt of a *nitrolic acid*, whilst the nitro-compounds of the **secondary** radicals yield a *dark blue* coloration, due to the formation of a *pseudo-nitrole* :



$$CH_3{\cdot}CH_2NO_2 + NOOH = CH_3{\cdot}C{<}^{NOH}_{NO_2} + H_2O.$$

Ethyl nitrolic acid
(Nitroacetaldoxime)



$$(CH_3)_2CHNO_2 + NOOH = (CH_3)_2C{<}^{NO}_{NO_2} + H_2O.$$

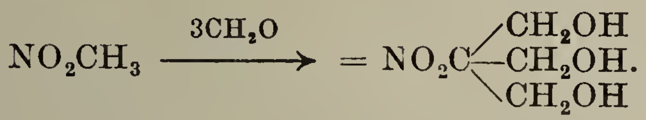
Propyl *pseudo*nitrole.

The nitro-compounds of **tertiary** radicals do not react with nitrous acid. Since the alcohols easily form iodides which react with silver nitrate, the preceding reactions serve as a means of distinguishing primary, secondary, and tertiary alcoholic radicals from one another (p. 136).

(4) Chlorine and bromine, acting on the alkali salts of primary and secondary nitroparaffins, produce chloro- and bromo-nitro-substitution products. In them the halogen atom occupies the same position as the nitro-group.

(5) Diazobenzene salts, acting on the alkali salts of the primary nitroparaffins, give nitrohydrazones (nitro-azoparaffins), *e.g. nitro-acetaldehyde hydrazone*, $CH_3C(NO_2):N\cdot NHC_6H_5$, results from potassium nitroethane and diazobenzene nitrate (Ber. **31**, 2626 ; see also Vol. II).

(6) *Reaction with aldehydes.*—Primary and secondary nitroparaffins unite with aldehydes in the presence of alkali carbonates to form nitro-alcohols. As many molecules of an aldehyde unite with one molecule of a nitro-paraffin as there are hydrogen atoms united to the carbon atom to which the nitro-group is attached. The nitro-alcohols, as obtained by this method, will be described with the polyatomic alcohols (C. 1897, II. 1000). Nitromethane and formaldehyde give rise to nitrobutyl glycerol, the parent substance for the synthesis of glycerol :



$$NO_2CH_3 \xrightarrow{3CH_2O} = NO_2C\begin{cases}CH_2OH\\CH_2OH.\\CH_2OH\end{cases}$$

αα-Haloid nitroparaffins also condense with aldehydes to form meso-halogen nitroparaffins, which will be described under the section of the nitrogen derivatives of the ketone-alcohols or ketols.

(7) *Carbon disulphide* reacts with the primary and secondary nitroparaffins to yield condensation products, *e.g.* nitromethane and CS_2 in the presence of alkali yield the salt of nitrodithioacetic acid (Ber. **52**, 542).

$$CH_2NO_2 + CS_2 \xrightarrow{NaOH} NaO\cdot NO:CH\cdot CS\cdot SH.$$

For compounds resulting from the action of sodium ethoxide and the alkyl iodides on the nitroethanes, see Ber. **21**, R. 58 and 710.

Zinc ethyl converts nitroethane into β-ethyl-β-*sec.*-butylhydroxylamine (Ber. **34**, 2500).

Primary mononitroparaffins : nitromethane, CH_3NO_2, b.p. 101°. *Sodium* and *potassium nitromethane* explode with great violence when they are heated ; this also occurs when these substances, dried in a desiccator, come into contact with traces of water (Ber. **27**, 3406). When mercuric chloride acts on sodium nitromethane, mercury fulminate is produced (*q.v.*) (Ann. **280**, 275). By the action of potassium hydroxide on nitromethane or of hydroxylamine hydrochloride on sodium nitromethane, *methazonic acid*, $CH_2NO_2\cdot CH:NOH$, m.p. 79°, the oxime of nitroacetaldehyde is obtained (*q.v.* See also Ber. **40**, 3435).

Nitroethane, CH_3CH_2NO, b.p. 113° ; reaction between the sodium salt, $CH_3CH:NOONa$, and benzoyl chloride leads to the formation of benzoylacetohydroxamic acid, $CH_3\cdot C(OH)NO\cdot COC_6H_5$, and not to the expected benzoyl-*iso*nitroethane (C. 1898, I. 564).

α-Nitropropane, $CH_3\cdot CH_2\cdot CH_2NO_2$, b.p. 130° ; α-*nitro*-n-*butane*, $CH_3\cdot CH_2\cdot$-

$CH_2 \cdot CH_2 \cdot NO_2$, b.p. 151° ; *nitro*iso*butane*, $(CH_3)_2CH \cdot CH_2NO_2$, b.p. 137–140° ; *nitro*-n-*octane*, $CH_3 \cdot [CH_2]_6 \cdot CH_2 \cdot NO_2$, b.p. 205–210°.

Secondary nitroparaffins.—*β-Nitropropane*, $CH_3 \cdot CH(NO_2) \cdot CH_3$, b.p. 118°. *$\beta$-Nitrobutane*, $C_2H_5CH(NO_2) \cdot CH_3$, b.p. 138°, is obtained from methylethyl carbinol in two optically active modifications. The persistence of the optical activity after conversion into the alkali salts is important (Ber. **60**, 1297 : see also p. 180).

Tertiary mononitroparaffins : *Tertiary nitrobutane*, $(CH_3)_3C \cdot NO_2$, b.p. 126° ; *β-nitro-β-methylbutane*, $(CH_3)_2C(NO_2)C_2H_5$, b.p. 150° (C. 1903, I. 625).

Nitro-olefines.—Nitro-alcohols, obtained by the condensation of aldehydes with nitromethane (comp. p. 378), give up water under the action of zinc chloride, and form nitro-olefines, $RCH : CHNO_3$; *nitro*iso*hexylene*, $(CH_3)_2CHCH_2CH : CHNO_2$, b.p. 80°/10 mm. ; *nitro-octylene*, $C_6H_{13}CH : CHNO_2$, b.p. 114°/8 mm. *Nitro*iso*butylene*, $(CH_3)C : CHNO_2$, is prepared by the action of fuming nitric acid on *iso*butylene ; and also by the abstraction of CO_2 by alkali from α-nitrodimethylacrylic acid. Reduction of the nitro-olefines results in the formation of the oximes of the paraffin aldehydes (p. 250) (C. 1903, II. 553).

Nitropropylene, $CH_2 : CH \cdot CH_2NO_2$, b.p. 88°/180 mm. (C. 1898, I. 192).

Halogen nitro-compounds result (1) from di-halogen paraffins in which two different halogen atoms are attached to two C-atoms in the same chain, such as $CH_2Cl \cdot CH_2 \cdot CH_2Br$, reacting with a mono-molecular quantity of silver nitrate ; (2) from nitroparaffins and Cl or Br ; (3) from nitro-alcohols and PCl_5. These substances are acidic in character when a H-atom is united to the same C-atom as the nitro-group. The remarks which have been made on the constitution of the salts of the mononitroparaffins hold good for the salts of the halogen-nitro-compounds (p. 179).

Chloronitromethane, CH_2ClNO_2, b.p. 122° ; *bromonitromethane*, b.p. 146° (Ber. **29**, 1823) ; *dibromonitromethane* (Ber. **29**, 1824).

$\alpha\alpha$-Chloronitroethane, $CH_3 \cdot CHClNO_2$, b.p. 124° ; *$\alpha\alpha$-bromonitroethane*, b.p. 146° ; *$\alpha\beta$-chloronitroethane*, $ClCH_2 \cdot CH_2NO_2$, b.p. 173° ; *$\alpha\alpha\alpha$-dibromonitroethane*, $CH_3 \cdot CBr_2NO_2$, b.p. 165°.

$\alpha\alpha$-Chloronitropropane, $CH_3CH_2CHClNO_2$, b.p. 141° ; *$\alpha\alpha$-bromonitropropane*, b.p. 165° ; *β-chloro-α-nitropropane*, b.p. 172° ; *α-chloro-β-nitropropane*, b.p. 170° ; *α-chloro-γ-nitropropane*, b.p. 197° ; *$\beta\beta$-chloronitropropane*, $CH_3CCl(NO_2) \cdot CH_3$, b.p. 133° ; *$\alpha\beta$-bromonitropropane*, b.p. 165° ; *$\alpha\alpha\alpha$-dibromonitropropane*, b.p. 185°.

Triiodonitroethylene, $CI_2 : CINO_2$, m.p. 109°, and *diiododinitroethylene*, $NO_2CI : CINO_2$, result from the action of fuming nitric acid or N_2O_3 on diiodo-acetylene and tetraiodoethylene respectively (Ber. **33**, 2190).

Following the scheme on which this work is planned, the nitro-halogen compounds should take their places after the aldehydes, ketones, carboxylic acids and glycols, according to the position of the substituting atom and group. It is, however, more convenient not to divide them in this way, except to deal with nitrochloroform (chloropicrin), CCl_3NO_2, and nitrobromoform (bromopicrin) in conjunction with CCl_4, CBr_4, CI_4.

The halogen atom in chloro- and bromo-mononitroparaffins can be replaced by alkyl groups by the action of zinc alkyls, whereby a homologous series of the mononitroparaffins can be built up (p. 179).

A 2. NITROSOPARAFFINS, *PSEUDO*NITROLES AND NITROLIC ACIDS

Compounds containing the group —NO are described as nitroso-compounds. The primary and secondary nitrosoparaffins cannot as a rule be isolated, as they change readily into the tautomeric oximino- or *iso*nitroso-compounds (*cf.* Ber. **35**, 2323).

$$RR'CH \cdot NO \rightleftarrows RR'C : NOH.$$

Tertiary nitrosoparaffins, on the other hand, are stable and are obtained by the oxidation of β-alkyl-hydroxylamines (p. 204).

The ketoximes, $R_2C : NOH$ (also acetaldoxime, $CH_3CH : NOH$), are changed by chlorine or bromine into *chloro-* or *bromo-nitrosoparaffins*, $R_2C<^{Br}_{NO}$; by N_2O_4 or nitric acid into nitronitrosoparaffins, $R_2C<^{NO_2}_{NO}$. The latter, also known as *pseudonitroles*, are also obtained (p. 184) by the action of nitrous acid on the secondary nitro-bodies, whilst the primary compounds yield *nitrolic acids*, $RC<^{NO_2}_{NOH}$, under the same treatment. The latter substances are desmotropic, and can also be formulated as nitrosonitronic acids, $RC<^{NOOH}_{NO}$

Nitrosoparaffins

The direct production of these bodies from the paraffins has not yet been brought about. Reduction of the nitroparaffins does not yield nitrosoparaffins, but a series of other bodies. Careful reduction gives rise first to β-alkylhydroxylamines, R·NHOH, which will be examined later together with other alkylhydroxylamine derivatives (p. 204). But the *tert.*-alkyl-β-hydroxylamines yield nitrosoparaffins by oxidation with chromic acid (Ber. **31**, 457) :

$$R_3C{\cdot}NO_2 \longrightarrow R_3C{\cdot}NHOH \longrightarrow R_3C{\cdot}NO.$$

The alkylamines, possessing a tertiary alkyl group, yield tertiary-nitrosoparaffins when oxidized by permonosulphuric acid, H_2SO_5, with the intermediate formation of β-alkylhydroxylamines :

$$R_3C{\cdot}NH_2 \longrightarrow R_3C{\cdot}NHOH \longrightarrow R_3C{\cdot}NO.$$

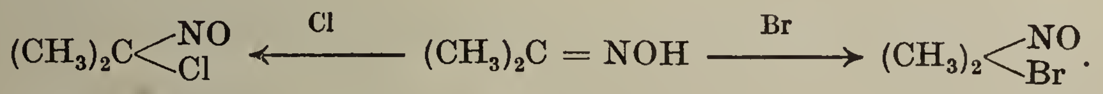
sec.-Alkyl-β-hydroxylamines are converted by oxidation into ketoximes or *iso*nitrosoparaffins (p. 204), whilst the primary compounds yield hydroxamic acids (Ber. **36**, 701).

Nitroso-compounds are *colourless* crystalline bodies, having an odour of camphor, and are very volatile. In the solid state they exist as double molecules, which are dissociated by heat or solution into the intensely *blue* coloured monomolecular condition. This phenomenon can be observed in many complex nitroso-bodies (Ber. **35**, 3090). Sunlight retards this dissociation. Nitroso-bodies on oxidation yield nitro-compounds.

tert.-**Nitroso*iso*butane,** $(CH_3)_3C{\cdot}NO$, which forms colourless (dimolecular) crystals, melting at 76° to a blue (monomolecular) liquid, and *tert.*-**nitroso*iso*pentane,** m.p. 50°, are prepared by the oxidation of *tert.*-butylamine and *tert.*-amylamine.

Nitrosooctane.—The compound $MeCH{\cdot}(CH_2)_2{\cdot}CMe_2NO$, m.p 54°, is obtained by reduction of the corresponding nitrooctane.

meso-**Halogen-nitrosoparaffins** are prepared by the action of chlorine and sodium hydroxide (C. 1906, I. 1692), or of bromine and pyridine (Ber. **35**, 3092) on ketoximes (see above) :



$$(CH_3)_2C<^{NO}_{Cl} \xleftarrow{Cl} (CH_3)_2C = NOH \xrightarrow{Br} (CH_3)_2<^{NO}_{Br}.$$

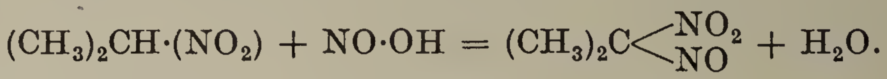
They are blue, very volatile bodies, of a sharp odour and are easily decomposed. Oxidation changes them into halogen-nitro-bodies (p. 182) ; with silver nitrite they give rise to the *pseudo*nitroles (see below).

meso-*Chloronitrosopropane*, $(CH_3)_2CCl{\cdot}NO$, b.p. 7°/18 mm., is formed from $(CH_3)_2CNOH$ and NaClO. An excess of the latter forms chloronitropropane (p. 182). *Bromonitrosopropane*, b.p. 41·5°/161 mm. *Bromonitrosobutane*, $C_2H_5C(CH_3)Br{\cdot}NO$, b.p. 28°/15 mm. *Bromonitrosodimethylbutane*, $(CH_3)_3C{\cdot}{\cdot}C(CH_3)Br{\cdot}NO$, m.p. 120°, with decomposition, form sky-blue crystals which can be sublimed.

αα-*Chloronitrosoethane*, $CH_3CHCl{\cdot}NO$, m.p. 65°, is prepared from acetaldoxime in hydrochloric acid solution and chlorine. It changes on fusion from colourless (dimolecular) plates, to a blue (monomolecular) liquid. This soon becomes colourless, owing to an isomeric change to acetohydroxamyl chloride (*q.v.*) which yields ααα-dichloronitrosoethane, $CH_3{\cdot}CCl_2{\cdot}NO$, a blue-coloured oil, b.p. 68°, by the further action of chlorine (Ber. **35**, 3113).

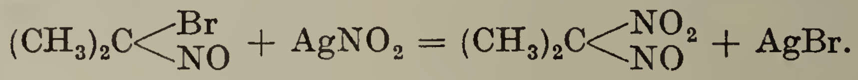
*Pseudo*Nitroles or *meso*-Nitronitrosoparaffins

As already described, the *pseudo*nitroles are prepared:
(1) By the action of nitrous acid on *sec.*-nitroparaffins (p. 180):



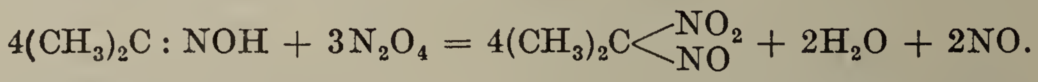
$$(CH_3)_2CH\cdot(NO_2) + NO\cdot OH = (CH_3)_2C{<}^{NO_2}_{NO} + H_2O.$$

(2) From *meso*-halogen-nitrosoparaffins and silver nitrite (Ber. **35**, 3093):



$$(CH_3)_2C{<}^{Br}_{NO} + AgNO_2 = (CH_3)_2C{<}^{NO_2}_{NO} + AgBr.$$

(3) By the action of N_2O_4 on the ketoximes, which is the simplest method of preparation (Ber. **34**, 1911):



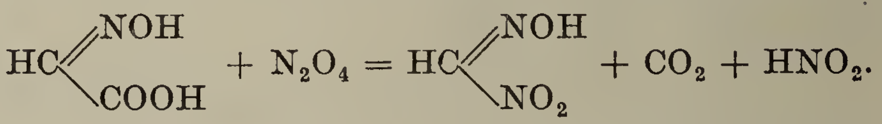
$$4(CH_3)_2C : NOH + 3N_2O_4 = 4(CH_3)_2C{<}^{NO_2}_{NO} + 2H_2O + 2NO.$$

The *pseudo*nitroles are pungent, colourless crystalline substances, dimolecular when in the solid state. On melting or solution they change into the deep-blue monomolecular form (Ber. **35**, 3094). They possess a neutral reaction, and are insoluble in water, alkalis, and acids. Chromic acid oxidizes them in glacial acetic acid solution to dinitro-compounds. Reduction with hydroxylamine in alkaline solution changes the *pseudo*nitroles into ketoximes (Ber. **29**, 88, 98).

*Propyl*pseudo*nitrole, nitronitrosopropane,* $(CH_3)_2C(NO_2)NO$, m.p. 76°, with decomposition, is changed by NH_2OH into tetramethyldinitroazoxymethane,
$O{=}N\cdot C(NO_2)(CH_3)_2$
$\|$ (Ber. **34**, 1913); *butyl*pseudo*nitrole, ββ-nitronitrosobutane,*
$N\cdot C(NO_2)(CH_3)_2$
m.p. 58°. For the higher homologues, see Ber. **29**, 94; **35**, 3095.

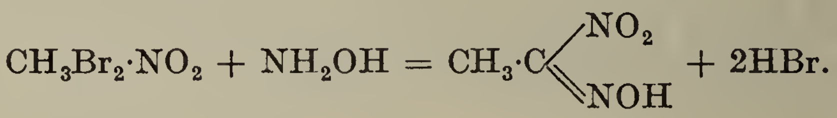
Nitrolic acids

As has already been described (p. 180), the nitrolic acids result from (1) the action of nitrous acid at the moment of its formation on the primary mononitro-compounds. (2) A more direct reaction is that of α-*iso*nitrosocarboxylic acids with N_2O_4 during which CO_2 is eliminated (C. 1903, II. 937):



$$HC{<}^{NOH}_{COOH} + N_2O_4 = HC{<}^{NOH}_{NO_2} + CO_2 + HNO_2.$$

(3) They can also be obtained from dibromomononitroparaffins and hydroxylamine:



$$CH_3Br_2\cdot NO_2 + NH_2OH = CH_3\cdot C{<}^{NO_2}_{NOH} + 2HBr.$$

These methods of formation represent the nitrolic acids as nitro-oximes, but their coloured salts are more probably derived from the tautomeric nitroso*iso*nitro compounds, $R\cdot C(NO) : NO\cdot OH$.

The nitrolic acids are solid, crystalline, colourless, or faintly yellow-coloured bodies, soluble in water, alcohol, ether, and chloroform. They are weak acids, and form very explosive salts with alkalis, yielding at the same time a dark-red colour. The erythronitrolic acid salts are changed by the action of sunlight and of heat to the colourless leuco-nitrolic acid salts from which the nitrolic acid cannot be regenerated (Ber. **31**, 2854). They are decomposed into hydroxylamine and the corresponding fatty acids by tin and hydrochloric acid. When heated with dilute sulphuric acid they split up into oxides of nitrogen and fatty acids. They are converted into esters when treated with acid chlorides (Ber. **27**, 1600: **29**, 1218). For further reactions, see the derivatives of the fatty acids.

Methylnitrolic acid, $CH(NO_2) : NOH$, m.p. 68° (dec.). *Ethylnitrolic acid,* m.p. 88° (dec.). *Propylnitrolic acid,* m.p. 60° (dec.).

Nitroalkyl*iso*nitramines, such as *nitroethyl*iso*nitramine,* $CH_3CH(NO_2)N_2O_2H$, result from the passage of NO into an alcoholic solution of an aliphatic mononitro-body, containing sodium ethoxide (Ann. **300**, 106).

Di*iso*nitramines, such as *methylene di*iso*nitramine,* $CH_2(N_2O_2H)_2$, result from the action of NO, in the presence of sodium ethoxide, on an alcoholic solution of a ketone which contains the CO group attached to a methyl or methylene group (Ann. **300**, 81).

A 3. DINITROPARAFFINS

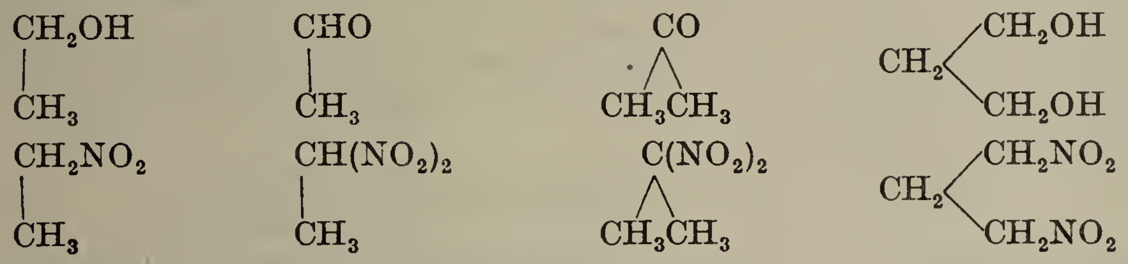
There are three classes of dinitroparaffins; the two nitro-groups may be joined—

(1) to one terminal carbon atom: *αα-dinitroparaffins* or *primary* dinitro-compounds;

(2) to an intermediate carbon atom: meso*dinitroparaffins* or *secondary* dinitro-compounds;

(3) to two different carbon atoms.

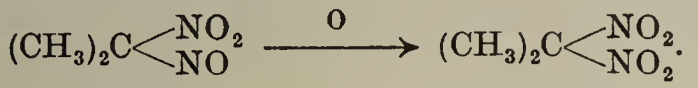
These three classes, according to the position of the groups, bear the same relations to aldehydes, ketones, and glycols as do the mononitroparaffins to the alcohols:



$$\begin{array}{cccc} \begin{array}{c} CH_2OH \\ | \\ CH_3 \end{array} & \begin{array}{c} CHO \\ | \\ CH_3 \end{array} & \begin{array}{c} CO \\ /\backslash \\ CH_3CH_3 \end{array} & CH_2{<}\begin{array}{l} CH_2OH \\ CH_2OH \end{array} \\ \begin{array}{c} CH_2NO_2 \\ | \\ CH_3 \end{array} & \begin{array}{c} CH(NO_2)_2 \\ | \\ CH_3 \end{array} & \begin{array}{c} C(NO_2)_2 \\ /\backslash \\ CH_3CH_3 \end{array} & CH_2{<}\begin{array}{l} CH_2NO_2 \\ CH_2NO_2 \end{array} \end{array}$$

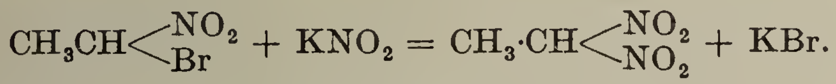
Notwithstanding these points of relationship, it is practicable to discuss the dinitroparaffins after the bromonitro- and nitrosonitro-bodies (*pseudo*nitroles).

Formation.—(1) By the oxidation of the *pseudo*nitroles with chromic acid meso*dinitroparaffins* are produced:



$$(CH_3)_2C{<}\begin{array}{l} NO_2 \\ NO \end{array} \xrightarrow{O} (CH_3)_2C{<}\begin{array}{l} NO_2 \\ NO_2 \end{array}.$$

(2) They result from the interaction of potassium nitrite and the bromonitroparaffins:



$$CH_3CH{<}\begin{array}{l} NO_2 \\ Br \end{array} + KNO_2 = CH_3{\cdot}CH{<}\begin{array}{l} NO_2 \\ NO_2 \end{array} + KBr.$$

(3) By the action of concentrated nitric acid on
- (*a*) secondary alcohols,
- (*b*) ketones,
- (*c*) mono-alkyl acetoacetic esters,

the carbon chain is torn asunder and αα-dinitroparaffins are formed (C. 1901, II. 334):

$$\begin{array}{rcl} (C_2H_5)_2CHOH & \longrightarrow & CH_3{\cdot}CH(NO_2)_2 \\ (C_2H_5)_2CO & \longrightarrow & CH_3{\cdot}CH(NO_2)_2 \\ CH_3CO{\cdot}CH(C_2H_5)CO_2C_2H_5 & \longrightarrow & CH_3{\cdot}CH_2{\cdot}CH(NO_3)_2. \end{array}$$

The action of alkyl iodides on the salts of the primary dinitroparaffins results in the production of *meso*dinitroparaffins (comp. Ann. **280**, 282).

(4) By the oxidation with nitric acid of saturated monocarboxylic acids, containing a tertiary carbon atom: *iso*butyric and *iso*valeric acids yield *meso*-dinitropropane:

$$(CH_3)_2CHCO_2H \longrightarrow (CH_3)_2C(NO_2)_2 \longleftarrow (CH_3)_2CH{\cdot}CH_2{\cdot}CO_2H.$$

The primary dinitro-bodies are acids in which the group $CH(NO_2)_2$ changes into $C(NO_2):NOOH$. The primary and secondary classes lose hydroxylamine when they are reduced with tin and hydrochloric acid. The former yield, at the same time, monocarboxylic acids, and the latter ketones (Ber. **23**, 3494).

Dinitromethane, $CH_2(NO_2)_2$, is a colourless volatile oil (Ber. **32**, 624). *αα-Dinitroethane*, $CH_3CH(NO_2)_2$, b.p. 185–186°; *αα-dinitropropane*, $CH_3CH_2CH(NO_2)_2$, b.p. 189°; *αα-dinitrohexane*, b.p. 212°; *ββ-dinitropropane*, $CH_3C(NO_2)_2CH_3$, m.p. 53°, b.p. 185·5°; *ββ-dinitrobutane*, $CH_3CH_2C(NO_2)_2{\cdot}CH_3$, b.p. 199°. For higher homologues, see Ber. **29**, 95.

tert.-Dinitroparaffins are obtained by the action of finely divided silver on the *meso*bromonitroparaffins (p. 182):

$$2R_2C(NO_2)Br + 2Ag = R_2C(NO_2){\cdot}C(NO_2)R_2 + 2AgBr.$$

βγ-Dinitro-βγ-dimethylbutane, $(CH_3)_2C(NO_2)\cdot C(NO_2)(CH_3)_2$, m.p. 211°, can be obtained by heating di*iso*propyl with dilute nitric acid (comp. also p. 178); and by electrolysis of the potassium salt of *sec.*-nitropropane. *γδ-Dinitro-γδ-dimethylhexane*, m.p. 80°, is prepared from *ββ*-bromonitrobutane (C. 1907, I. 230). *αγ-Dinitropropane*, $NO_2CH_2CH_2CH_2NO_2$, is obtained as an unstable oil from trimethylene iodide and silver nitrite. *αδ-Dinitrodi*isob*utyl*, $NO_2C(CH_3)_2CH_2CH_2C(CH_3)_2NO_2$, m.p. 125°, is prepared from di*iso*butyl by heating it with dilute nitric acid. *αζ-Dinitrodi*iso*amyl*, $(CH_3)_2C(NO_2)[CH_2]_4C(NO_2)(CH_3)_2$, m.p. 102°, is similarly prepared (Ber. **25**, 2638 : **28**, 1858 : C. 1906, II. 312 *et seq.*). These dinitroparaffins yield the corresponding diamines when reduced.

Halogendinitroparaffins.—*Tetrachlorodinitroethane*, $NO_2CCl_2\cdot CCl_2NO_2$, is obtained from tetrachloroethylene and carefully dried nitrogen tetroxide (J. Phys. Chem. **23**, 578).

A 4. POLYNITROPARAFFINS

Trinitromethane, *nitroform*, $CH(NO_2)_3$, m.p. 15°, was first prepared by the action of water on trinitroacetonitrile, which gave at the same time CO_2 and ammonium *iso*nitroform. It is also prepared from tetranitromethane by the action of alcoholic potassium hydroxide or ammonia with the simultaneous production of ethyl nitrate:

$$C(NO_2)_3\cdot CN + 2H_2O = (NO_2)_2C : NOONH_4 + CO_2.$$
$$C(NO_2)_4 + C_2H_5OK = (NO_2)_2C : NOOK + C_2H_5O\cdot NO_2.$$

It also results from the interaction of acetylene (p. 110) and nitric acid.

It forms colourless crystals, dissolving to a colourless solution in non-aqueous solvents, but turning yellow in water. The salts are also of a yellow colour, and are probably derived from *iso*nitroform $(NO_2)_2C : NOOH$ (*cf.* p. 179). In non-dissociating solvents a colourless mercury salt, $(NO_2)_3C\cdot\frac{1}{2}Hg$, is formed, but in dissociating liquids this exists as yellow $(NO_2)_2C : NOO\cdot\frac{1}{2}Hg$ (Ber. **38**, 973). Thus, in water it assumes the *iso-* or *aci-* condition, and is a very strong mono-basic acid.

Free trinitromethane is volatile in steam, and explodes violently on heating. The freshly prepared potassium salt explodes at 97–99°, and spontaneously decomposes, on keeping, in dry air. The ammonium compound crystallizes in yellow needles, and explodes mildly at 200°. The silver salt dissolves easily in water and in alcohol (Ber. **32**, 628).

Trinitroethane, $CH_3C(NO_2)_3$, m.p. 56°, is obtained from the silver compound of trinitromethane and iodomethane; and also from methylmalonic acid and nitric acid. It is insoluble in water. Potassium hydroxide solution changes it into potassium dinitroethane, whilst potassium methoxide produces dinitroethyl methyl ether, $CH_3OCH_2CH(NO_2)_2$ (Ber. **36**, 434).

Chlorotrinitromethane, *chloronitroform*, $CCl(NO_2)_3$, m.p. $\dotplus$ 4·5°, b.p. 32°/10 mm., is obtained by passing chlorine into an ethereal suspension of potassium nitroform (Ber. **54**, 1483).

Bromonitroform, *bromotrinitromethane*, $C(NO_2)_3Br$, m.p. 12°, is produced when bromine and nitroform remain in contact for some days in the sunlight. A quicker method is to pass bromine into an aqueous solution of the mercury salt of nitroform. It can be obtained similarly to the chloro- compound. It is volatile in steam without decomposition.

Tetranitromethane, $(CNO_2)_4$, m.p. 13°, b.p. 126°, $D._4^{13}$ = 1·65, is obtained from diacetyl orthonitric acid and acetic anhydride (Ber. **36**, 2225); also by warming nitroform with a mixture of fuming nitric acid and sulphuric acid. It is a colourless oil, insoluble in water, but easily soluble in alcohol and ether. It is very stable and distils without exploding. On the other hand, when mixed with other carbon compounds it explodes violently on ignition (*cf.* Z. angew. Chem. **33**, 245 : Chem. Ztg. **44**, 497). The decomposition with sodium ethoxide sometimes takes place explosively (Ber. **46**, 2537).

With aqueous alkali, it decomposes either into the alkali salt of nitroform and a nitrate or into a nitrite and an alkali carbonate, according to the concentration of the alkali. *Constitution of tetranitromethane*, see Ber. **37**, 1779 : **52**, 400.

With many unsaturated compounds and aromatic compounds, and with piperidine, tetranitromethane yields yellow to brown-red colorations, and can be used as a reagent for detecting double bonds (Ber. **42**, 4324 : J. pr. Chem. [2] **84**, 489). In the presence of pyridine it can be used for the nitration of unsaturated side-chains (Ber. **55**, 1751).

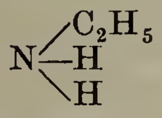
Tetranitroethane is obtained as a dipotassium salt, $KOON : C(NO_2) \cdot C(NO_2) : NOOK$, from bromopicrin, CBr_3NO_2, and potassium cyanide. It is decomposed by cold dilute sulphuric acid, forming dinitromethane (Ber. **35**, 4288).

Hexanitroethane, $(NO_2)_3C \cdot C(NO_2)_3$, m.p. 142° (partial dec.), is formed by the action of a mixture of nitric and sulphuric acids on potassium tetranitroethane. It explodes on rapid heating, but is insensitive to blows (Ber. **47**, 961).

B. AMINES AND ALKYLAMMONIUM DERIVATIVES

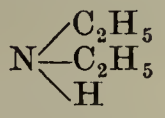
Amines are substances formed by replacement of the hydrogen atoms in ammonia by alkyl groups.

According as one, two, and three atoms are substituted, there result the *primary*, *secondary*, and *tertiary* amines :



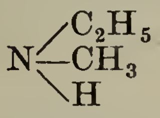
$N \begin{matrix} \diagup C_2H_5 \\ -H \\ \diagdown H \end{matrix}$

Ethylamine.



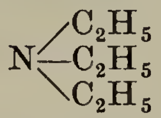
$N \begin{matrix} \diagup C_2H_5 \\ -C_2H_5 \\ \diagdown H \end{matrix}$

Diethylamine.



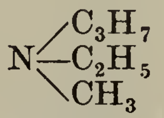
$N \begin{matrix} \diagup C_2H_5 \\ -CH_3 \\ \diagdown H \end{matrix}$

Methylethylamine.



$N \begin{matrix} \diagup C_2H_5 \\ -C_2H_5 \\ \diagdown C_2H_5 \end{matrix}$

Triethylamine.



$N \begin{matrix} \diagup C_3H_7 \\ -C_2H_5 \\ \diagdown CH_3 \end{matrix}$

Methylethylpropylamine.

Among the secondary and tertiary amines, may be distinguished simple amines, those with similar alcohol radicals, and mixed amines, those containing different alcohol radicals (comp. simple and mixed ethers, p. 154). Derivatives also exist which correspond with the ammonium salts and hypothetical ammonium hydroxide, NH_4OH :

$(C_2H_5)_4NCl$.	$(C_2H_5)_4N \cdot OH$.
Tetraethylammonium chloride.	Tetraethylammonium hydroxide.

known as the quaternary alkylammonium compounds. In these compounds the group $R_4N \cdot$ plays the part of an alkali metal, and by electrolysis of tetraethylammonium iodide in liquid ammonia at − 70°, Schlubach has obtained the free tetraethylammonium at the cathode. It forms deep-blue solutions in liquid ammonia, and behaves very like metallic potassium (Ber. **54**, 2811).

Schlenk has prepared a new series of compounds by the action of sodium alkyls on tetramethylammonium chloride (Ber. **49**, 603 : **50**, 274, 276) :

$$R \cdot Na + (CH_3)_4N \cdot Cl \xrightarrow{\qquad} NaCl + (CH_3)_4N \cdot R.$$

In these compounds the radical R takes the place of the electronegative chlorine, and the compounds behave as electrolytes in absolute pyridine and are hydrolysed by water according to the equation :

$$R \cdot NMe_4 + H_2O \xrightarrow{\qquad} R \cdot H + NMe_4OH.$$

This affords further evidence that the fifth valency in pentavalent nitrogen compounds is different from the other four, and, indeed, there is no evidence that nitrogen can ever have more than four " covalencies." The fifth must always be an electrovalency.

Isomerism of amines.—The isomerism of the alkylamines depends on (*a*) the different combinations of alkyl groups attached to the nitrogen atom—" metamerism "—*e.g.* diethylamine, $(C_2H_5)_2NH$, and methylpropylamine, $(CH_3)(C_3H_7)NH$, both with the same empirical formula, $C_4H_{11}N$, and (*b*) isomerism within the various alkyl groups.

The tertiary amines containing three different alkyl groups have not been resolved into stereoisomeric forms, in spite of very numerous attempts (see Ber. **57**, 1744).

History.—The existence of alkylamines, or alcohol bases, was very definitely predicted by *Liebig* in 1842 (Hdw. **1**, 689). In 1849 *Wurtz* discovered a method for the preparation of primary amines, which consisted in decomposing *iso*cyanic esters with aqueous potassium hydroxide. This was a discovery of the greatest importance for the development of organic chemistry. Shortly afterwards, in 1849, *A. W. Hofmann*, by the action of alkyl halides on ammonia, discovered a reaction which made possible the preparation of all the classes described in the preceding paragraphs: *primary, secondary, tertiary amines*, and the *alkylammonium* bases. This afforded the experimental basis for the introduction of the ammonia type into organic chemistry (comp. p. 22). Since that time numerous other methods have been found, particularly for the primary amines.

Methods of Formation of Amines

The principal methods of formation of amines fall into the four following classes:

I. From alkyl halides (and other esters), the halogen atom being replaced by an amino group.

II. By reduction of various nitrogen compounds.

III. From *iso*cyanates or *iso*thiocyanates and alkalis.

IV. Various other methods.

I. From Alkyl Halides and other Esters

(1) The iodides, the bromides, or the chlorides of the alcohol radicals are heated to 100°, in sealed tubes, with alcoholic ammonia (A. W. Hofmann, 1849). Two reactions occur here: first, the alkyl halides combine with the ammonia, forming alkylammonium salts, which are then partially decomposed by excess of ammonia into alkylamines, with which the alkyl halides again react, *e.g.*:

$$
\begin{aligned}
NH_3 + C_2H_5I &= NH_2(C_2H_5)HI \xrightarrow{NH_3} NH_2C_2H_5 + NH_4I. \\
NH_2C_2H_5 + C_2H_5I &= NH(C_2H_5)_2HI \xrightarrow{NH_3} NH(C_2H_5)_2 + NH_4I. \\
NH(C_2H_5)_2 + C_2H_5I &= N(C_2H_5)_3HI \xrightarrow{NH_3} N(C_2H_5)_3 + NH_4I. \\
N(C_2H_5)_3 + C_2H_5I &= N(C_2H_5)_4I.
\end{aligned}
$$

The final product consists of the hydroiodides of primary, secondary, and tertiary amines, as well as the quaternary ammonium compounds. The amines are best obtained on a large scale by the action of ammonia on the alkyl bromides (Ber. **22**, 700).

Potassium and sodium hydroxides decompose the salts of the alkylamines, with the liberation of the free bases, whereas the quaternary tetra-alkylammonium salts are *not* decomposed by alkali hydroxide, and can thus be easily separated from the primary, secondary, and tertiary amines (Ber. **20**, 2224).

It is remarkable that the iodides of primary and secondary alkyl radicals yield amines, whilst the tertiary alkyl iodides split off hydrogen iodide and pass into olefines. On the further alkylation of primary and secondary amines by means of alkyl bromides, see Ber. **38**, 1539.

(2) The *esters of nitric acid,* when heated to 100° with alcoholic ammonia, react in a manner analogous to the alkyl iodides :

$$C_2H_5\cdot O\cdot NO_2 + NH_3 = C_2H_5\cdot NH_2 + HNO_3.$$

This reaction is often very convenient for the preparation of the primary amines (Ber. **14,** 421).

(3) Tertiary amines are produced when primary and secondary bases are heated with an excess of potassium methyl sulphate (Ber. **24,** 1678) :

$$(C_2H_5)_2NH + CH_3OSO_3K = (C_2H_5)_2NCH_3 + HOSO_3K.$$

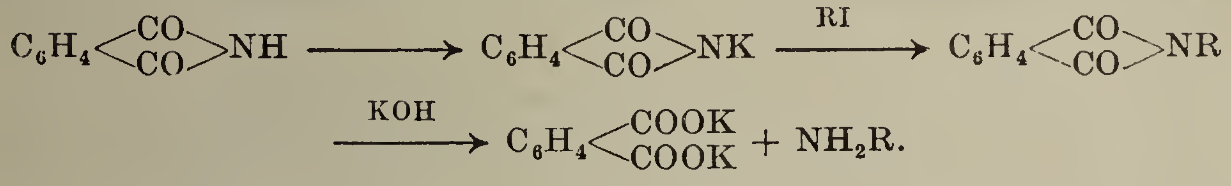
(4) Mono-, di, and tri-alkylamines are obtained by directly heating the alcohols to 250–260° with zinc-ammonium chloride, $ZnCl_2\cdot NH_3$ (Ber. **17,** 640).

(5) The methylation of ammonia and amines can easily be carried out by means of two reagents—dimethyl sulphate (p. 167) and formaldehyde (p. 223) (comp. Ber. **38,** 880 : Ann. **327,** 104 : C. 1906, II. 1716), *e.g.*

$$NH_3 + (CH_3)_2SO_4 \xrightarrow{0^\circ} NH_2\cdot CH_3 + H(CH_3)SO_4.$$

$$2NH_4Cl + 9CH_2O \xrightarrow{120^\circ} 2N(CH_3)_3\cdot HCl + 3CO_2 + 3H_2O.$$

(6) *By the use of phthalimide.*—Phthalimide (see Vol. II) forms a potassium derivative, which, when acted on by an alkyl halide, readily yields *N*-alkylphthalimides. These are readily hydrolysed into phthalic acid and the required primary amine. This method is a useful one for preparing pure primary amines, unmixed with secondary (Gabriel, Ber. **20,** 2224 : **24,** 3104).



$$C_6H_4\left<\begin{matrix}CO\\CO\end{matrix}\right>NH \longrightarrow C_6H_4\left<\begin{matrix}CO\\CO\end{matrix}\right>NK \xrightarrow{RI} C_6H_4\left<\begin{matrix}CO\\CO\end{matrix}\right>NR \xrightarrow{KOH} C_6H_4\left<\begin{matrix}COOK\\COOK\end{matrix}\right> + NH_2R.$$

II. By reduction of various Nitrogen Compounds

(7) *Nitro compounds.*—Amines are formed by the reducing action of nascent hydrogen, from zinc and hydrochloric acid on the nitroparaffins (p. 180), when the alkyl hydroxylamines appear as intermediate products, or on the halogen mononitroparaffins :

$$\begin{aligned}CH_3NO_2 + 4H &= CH_3NHOH + H_2O.\\ CH_3\cdot NO_2 + 6H &= CH_3\cdot NH_2 + 2H_2O.\\ CCl_3NO_2 + 12H &= CH_3NH_2 + 2H_2O + 3HCl.\end{aligned}$$

This method is particularly important in the manufacture of commercially valuable primary aromatic amines—*e.g.* aniline, $C_6H_5NH_2$—from the readily accessible aromatic nitro-bodies. *Zinin* discovered the method when investigating the reduction of nitrobenzene, $C_6H_5NO_2$, and *V. Meyer* applied it to the aliphatic nitro-derivatives.

The isomeric nitrites are not reduced, but hydrolysed, by this method. However, by leading their vapour mixed with hydrogen over heated finely-divided nickel they are reduced to amines, probably undergoing previous isomerization to nitro-compounds (Ann. Chim. Phys. [8] 25, 125).

(8) *Azomethine* (—C : N—) *compounds.*—(*a*) From *aldehyde-alkylimines* with sodium in absolute alcohol (Ber. **29,** 2110 : **43,** 2031).

$$R\cdot CH : NR' + 2H \longrightarrow R\cdot CH_2\cdot NHR'$$

(*b*) From *aldehyde-ammonias*, by zinc dust and HCl (Ber. **27**, R. 437).

(*c*) From *phenylhydrazones* (Tafel) and *oximes* (Goldschmidt) of aldehydes and ketones by sodium amalgam and glacial acetic acid (Ber. **19**, 1925, 3232 : **20**, 505 : **22**, 1854).

$$RR'C:N\cdot NHC_6H_5 \longrightarrow RR'CH\cdot NH_2 + C_6H_5NH_2$$
$$RR'C:NOH \longrightarrow RR'CH\cdot NH_2$$

Reaction (*a*) yields secondary amines, whilst (*b*) and (*c*) give rise to primary amines, together with some secondary and tertiary amines. The above reactions can be carried out with molecular hydrogen in presence of finely divided nickel or copper (C. 1905, II. 540) ; also by electrolytic hydrogen in acid solution (Ber. **42**, 3994).

(9) *Nitriles.*—These can be reduced to amines by means of sodium and alcohol (Ber. **18**, 2957 : **19**, 783 : **22**, 1854) or catalytically by hydrogen and palladium or nickel (Ber. **56**, 1988).

$$\underset{\substack{\text{Acetonitrile}\\ \text{(methyl cyanide).}}}{CH_3CN} + 4H \longrightarrow \underset{\text{Ethylamine.}}{CH_3CH_2NH_2}$$

Secondary and tertiary amines are also produced as by-products. This reaction forms an important step in the synthesis of a carbon compound containing *n + 1* carbon atoms from one containing *n*.

(10) *Acid amides and thioamides.*—The amides can be reduced by sodium and boiling amyl alcohol (C. 1899, II, 703) and the thioamides by aluminium amalgam in alcoholic or ethereal solution (Ann. **431**, 190) :

$$R\cdot CO\cdot NH_2 + 4H \longrightarrow H_2O + R\cdot CH_2\cdot NH_2$$

III. From iso*cyanates and* iso*thiocyanates*

(11) *Alkyl* iso*cyanates* or iso*thiocyanates* when heated with alkalis yield pure primary amines (*Wurtz*, 1849) :

$$R\cdot N:CO + 2KOH \longrightarrow R\cdot NH_2 + K_2CO_3$$
$$R\cdot N:CS + 3KOH \longrightarrow R\cdot NH_2 + KSH + K_2CO_3.$$

Alcohols can be conveniently converted into the corresponding pure primary amine by converting them into the iodide, treating this with silver cyanate, and then distilling the product with solid sodium hydroxide from the oil-bath (Ber. **10**, 131).

(12) *Carbylamines* (iso*nitriles*) also yield amines when heated with dilute hydrochloric acid, formic acid being split off (A. W. Hofmann) :

$$R\cdot NC + 2H_2O \longrightarrow R\cdot NH_2 + H\cdot COOH.$$

IV. Various other methods

(13) *From amino-acids.*—Amino-acids are broken down with the formation of amines when they are heated with baryta. The formation of amines from amino-acids by the action of various micro-organisms is of great importance :

$$R\cdot CH(NH_2)\cdot COOH \longrightarrow R\cdot CH_2\cdot NH_2 + CO_2.$$

(14) *From aromatic* p-*nitrosamines.*—The decomposition of the

secondary and tertiary aromatic *p*-nitrosamines into salts of nitrosophenol (*q.v.*), by means of potassium hydroxide, affords a means of preparing primary and secondary amines; *p*-nitrosodimethylaniline yields dimethylamine:

$$NO{\cdot}C_6H_4{\cdot}N(CH_3)_2 + KOH = NH(CH_3)_2 + NO{\cdot}C_6H_4{\cdot}OK.$$

(15) *From acid amides.*—The conversion of the amides of the mono-carboxylic acids into amines containing an atom less of carbon (*A. W. Hofmann*, Ber. **18**, 2734: **19**, 1822), can be effected by means of potassium hydroxide and bromine.

This reaction constitutes an intermediate step in the decomposition of the saturated monocarboxylic acids, because the primary amines can be changed to alcohols, and the latter be oxidized to carboxylic acids, containing an atom less of carbon than the fatty acids, whose amides constituted the parent substance.

The reaction proceeds in four stages. The first is the formation of the "bromoamide" of the fatty acid. The second stage is the formation of an unstable intermediate compound, which (III) undergoes isomerization leading to the formation of an alkyl *iso*cyanate, which, lastly, is broken down by excess of alkali into the primary amine and potassium carbonate (Ber. **35**, 3579: J. pr. Chem. [2] **73**, 228: C. 1903, I. 489):

$$\begin{aligned}
&\text{I. } C_2H_5CONH_2 + Br_2 + KOH = C_2H_5CONHBr + KBr + H_2O.\\
&\text{II. } C_2H_5CONHBr + KOH = C_2H_5{\cdot}CON< + KBr + H_2O.\\
&\text{III. } C_2H_5{\cdot}CON< \text{ isomerizes to } C_2H_5{\cdot}N:C:O.\\
&\text{IV. } C_2H_5NCO + 2KOH = C_2H_5NH_2 + K_2CO_3.
\end{aligned}$$

The bromoamide and the alkyl *iso*cyanate can both be isolated under special conditions.

If one molecule of bromine acts on two of the amide, compound ureas (*q.v.*) are formed—acetamide yields acetyl monomethyl urea.

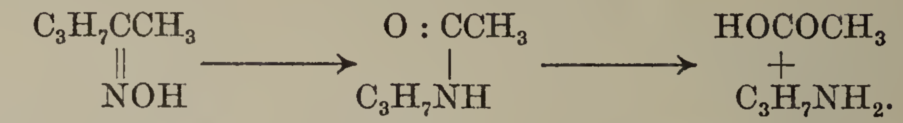
The amides of the fatty acids containing more than 5 C-atoms yield at the same time an increasing quantity of the nitrile of the next lower acid, *e.g.* $C_8H_{17}CONH_2$ gives $C_7H_{15}{\cdot}CN$. If, however, the higher bromamide or chloramide is converted by sodium methoxide into the corresponding urethane and the latter is hydrolysed, a good yield of the higher primary amine is obtained (Ber. **30**, 898: C. 1899, II. 363).

(16) *From acid azides.*—Similar, too, is the formation of primary amines from acid-azides and alcohol. The corresponding acid is converted into its ester, the ethoxy-group is then replaced with $(NH{\cdot}NH_2)$ by means of hydrazine hydrate, the acid-*hydrazide*, $R{\cdot}CO{\cdot}NH{\cdot}NH_2$, is changed by nitrous acid into the *azide* $R{\cdot}CO{\cdot}N_3$, which is boiled with water or alcohol, and the resulting urea or urethane acted on with concentrated hydrochloric acid, when the alkylized base is liberated (*Curtius*, Ber. **27**, 779: **29**, 1166). An *iso*cyanate is a probable intermediate compound in this reaction also.

$$R{\cdot}CO{\cdot}N_3 \xrightarrow{C_2H_5OH} R{\cdot}NH{\cdot}CO{\cdot}OC_2H_5 \xrightarrow{HCl} R{\cdot}NH_2.$$

(17) *From ketoximes.*—When the oximes of ketones are treated with certain reagents, such as acetyl chloride, they undergo an intramolecular rearrangement with the formation of a substituted acid amide. This can be hydrolysed to yield the corresponding primary

amine (Ber. **42**, 2340 : **44**, 1207). The mechanism of this "*Beckmann transformation*" is discussed on p. 268.



$$\underset{\text{NOH}}{\overset{C_3H_7CCH_3}{\|}} \longrightarrow \underset{C_3H_7NH}{\overset{O : CCH_3}{|}} \longrightarrow \underset{C_3H_7NH_2.}{\overset{HOCOCH_3}{+}}$$

Methyl propyl ketoxime. Acetpropylamide. Propylamine.

Another related reaction is the transformation of hydroxamic acids (compare Benzhydroxamic acid, Vol. II).

Properties and Reactions of the Amines

The amines are very similar to ammonia in their behaviour. The lower members are gases, possessing an ammoniacal odour, and are very readily soluble in water. Their combustibility distinguishes them from ammonia, a property to which Wurtz drew attention in connection with ethylamine (Ber. **20**, R. 928). The higher members are liquids, readily soluble in water, and only the highest dissolve with difficulty. Many amines possess the power of forming hydrates with water, accompanied by very considerable rise in temperature. They can be dried over potassium carbonate. Most of the oily hydrates contain one molecule of water for each nitrogen atom. This can only be removed by means of potassium hydroxide (Ber. **27**, R. 579), or by distillation over barium oxide. Like ammonia, they unite directly with acids to form salts, which differ from ammoniacal salts by their solubility in alcohol. They combine with some metallic chlorides, and form compounds perfectly analogous to the ammonium double salts ; *e.g.* :

$$[N(CH_3)H_3Cl]_2PtCl_4. \qquad N(CH_3)H_3Cl,AuCl_3. \qquad [N(CH_3)_3HCl]_2HgCl_2.$$

The compounds with picrolonic acid, picric acid and other aromatic poly-nitro compounds are of importance, and are frequently of value in the identification of amines.

The ammonia in the alums, the cuprammonium salts and other compounds may be replaced by amines.

The *dissociation constant* of the amines is greater than that of ammonia, and increases with the number of alkyls introduced (J. pr. Chem. [2] **33**, 352 : Ann. **345**, 256 : Z. physik. Chem. **77**, 385 : J.C.S. **101**, 1635).

The reactivity of the primary and secondary amines, as compared with the tertiary amines, is dependent on the ease with which the ammonia hydrogen atoms, not substituted by alcohol radicals, are replaced ; hence, the primary and the secondary amines in many reactions behave like ammonia.

A primary amine is distinguished from a secondary amine, and this from a tertiary amine, by treating the amine alternately with iodomethane and potassium hydroxide until all the hydrogen atoms in the ammonia present are replaced by methyl groups. Whether the latter have entered, and what their number may be, is most conveniently determined by the analysis of the platinum double chloride of the base previous to and after the action of the iodomethane. If two methyl groups have entered, then the amine was primary ; if one methyl group has entered, then the base was secondary ; and should the base remain unchanged, then it is tertiary in its character.

Tertiary, secondary, and primary amines may also be obtained by the dry distillation of the halogen salts of the ammonium bases, such as the methylammonium hydrochlorides :

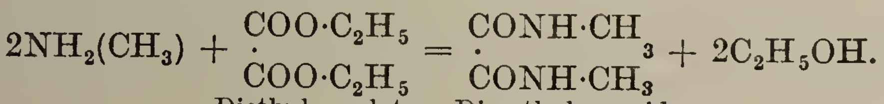
$$\begin{aligned} N(CH_3)_4Cl &= N(CH_3)_3 + CH_3Cl \\ N(CH_3)_3HCl &= NH(CH_3)_2 + CH_3Cl \\ NH(CH_3)_2HCl &= NH_2(CH_3) + CH_3Cl, \text{ etc.} \end{aligned}$$

These reactions serve for the commercial production of methyl chloride (p. 164) from trimethylamine.

Reactions

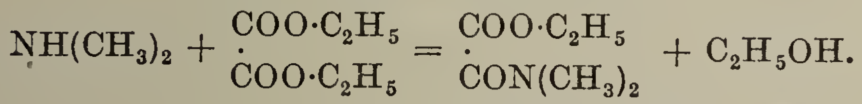
(1) Primary and secondary amines, like ammonia, react with acid esters, forming acid mono- and di-alkyl amides (*q.v.*) and alcohols. *A. W. Hofmann* based a method for the separation of primary, secondary, and tertiary amines upon their behaviour towards diethyl oxalate (Ber. 8, 760).

The mixture of the dry bases is treated with diethyl oxalate, when the primary amine, *e.g.* methylamine, is changed to dimethyloxamide, which is soluble in water, dimethylamine is converted into the ester of dimethyloxamic acid (see oxalic acid compounds), and trimethylamine is not acted on :



$$2NH_2(CH_3) + \begin{array}{l} COO{\cdot}C_2H_5 \\ \cdot \\ COO{\cdot}C_2H_5 \end{array} = \begin{array}{l} CONH{\cdot}CH_3 \\ \cdot \\ CONH{\cdot}CH_3 \end{array} + 2C_2H_5OH.$$

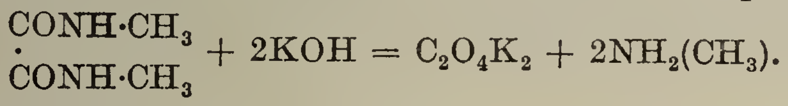
Diethyl oxalate. Dimethyloxamide.



$$NH(CH_3)_2 + \begin{array}{l} COO{\cdot}C_2H_5 \\ \cdot \\ COO{\cdot}C_2H_5 \end{array} = \begin{array}{l} COO{\cdot}C_2H_5 \\ \cdot \\ CON(CH_3)_2 \end{array} + C_2H_5OH.$$

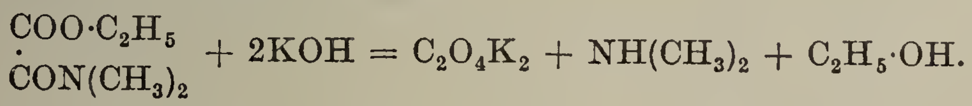
Dimethyloxamic ester.

When the reaction-product is distilled, the unaltered trimethylamine passes over. Water will extract the dimethyloxamide from the residue ; on distillation with potassium hydroxide it changes into methylamine and potassium oxalate :



$$\begin{array}{l} CONH{\cdot}CH_3 \\ \cdot \\ CONH{\cdot}CH_3 \end{array} + 2KOH = C_2O_4K_2 + 2NH_2(CH_3).$$

The insoluble dimethyl oxamic ester is converted, by distillation with potassium hydroxide, into dimethylamine :



$$\begin{array}{l} COO{\cdot}C_2H_5 \\ \cdot \\ CON(CH_3)_2 \end{array} + 2KOH = C_2O_4K_2 + NH(CH_3)_2 + C_2H_5{\cdot}OH.$$

The behaviour of the primary and secondary amines towards formaldehyde can be utilized for their separation from one another (Ber. 29, R. 520).

(2*a*) The secondary aliphatic amines, *e.g.* diethylamine (also piperidine), are readily acted on by a series of non-metallic chlorides, non-metallic oxy- and sulpho-chlorides, as well as chlorides of inorganic acids. The dialkylamine residue replaces one or all of the chlorine atoms. The products are dialkyl amides (Ber. 29, 710).

Thionyl chloride replaces both the hydrogen atoms in primary amines by the thionyl residue, with the production of thionylamines, the alkylated imides of sulphurous acid (Michaelis), which bear the same relation to sulphur dioxide that the *iso*cyanic esters do to carbon dioxide.

Nitrosyl chloride, NOCl, and nitrosyl bromide, NOBr, produce from primary amines alkyl chlorides and bromides, with the formation of water and nitrogen; under similar treatment secondary amines yield nitrosamines (C. 1898, II. 887: Ber. **40**, 1052).

The following arrangement, taking diethylamine as example, affords a review of these reactions:

$\begin{matrix}SCl\\ \cdot \\ SCl\end{matrix} \longrightarrow$	$\begin{matrix}S—N(C_2H_5)_2\\ \cdot \\ S—N(C_2H_5)_2\end{matrix}$	Dithio-diethylamine.
$SCl_2 \longrightarrow$	$S{<}\begin{matrix}N(C_2H_5)_2\\N(C_2H_5)_2\end{matrix}$	Monothio-diethylamine.
$SOCl_2 \longrightarrow \nearrow$	$SON(C_2H_5)$	Thionyl-ethylamine.
$\searrow$	$SO{<}\begin{matrix}N(C_2H_5)_2\\N(C_2H_5)_2\end{matrix}$	Thionyl-diethylamine.
$SO_2Cl_2 \longrightarrow$	$SO_2{<}\begin{matrix}N(C_2H_5)_2\\N(C_2H_5)_2\end{matrix}$	Sulphuryl- or Sulpho-diethylamine.
$NOCl \longrightarrow$	$NO{\cdot}N(C_2H_5)_2$	Nitroso-diethylamine.
$PCl_3 \longrightarrow$	$PCl_2N(C_2H_5)_2$	Diethylamine-chlorophosphine.
$POCl_3 \longrightarrow \nearrow$	$POCl_2N(C_2H_5)_2$	Diethylamine-oxychlorophosphine.
$\searrow$	$PO[N(C_2H_5)_2]_3$	Tridiethylamine-phosphine-oxide.
$PSCl_3 \longrightarrow$	$PSCl_2N(C_2H_5)_2$	Diethylamine-sulphochlorophosphine.
$BCl_3 \longrightarrow$	$BCl_2N(C_2H_5)_2$	Diethylamine-chloroboride.
$SiCl_4 \longrightarrow$	$SiCl_3N(C_2H_5)_2$	Diethylamine-chlorosilicide.

(2*b*) Primary and secondary amines behave like ammonia towards organic acid chlorides—*e.g.* acetyl chloride—forming mono- and di-alkyl amides.

The reaction proceeds twice as fast in the case of the primary amines as in that of the secondary.

Primary, secondary, and tertiary bases can be separated from each other by means of benzene sulphochloride, $C_6H_5{\cdot}SO_2Cl$. In the presence of alkalis tertiary amines do not react; under similar conditions secondary amines yield insoluble di-alkylsulphonamides, $C_6H_5SO_2NR_2$, whilst primary amines form mono-alkyl-sulphonamides, $C_6H_5SO_2NHR$, which yield soluble sodium salts $C_6H_5SO_2{\cdot}NNaR$ with aqueous sodium hydroxide, but which are insoluble when produced by metallic sodium under ether. Dibenzenesulpho-alkyl amides $(C_6H_5SO_2)_2NR$ occur as subsidiary products which form similar sodium salts $C_6H_5SO_2N{\cdot}NaR$ when warmed with sodium alcoholate (Ber. **38**, 908: C. 1906, II. 15).

(2*c*) The primary and secondary amines react similarly with 2 : 4-dinitro-bromobenzene or 2 : 4 : 6-trinitrochloro-benzene as with acid chlorides (Ber. **18**, R. 540), giving rise to di- and trinitrophenyl alkyl- and di-alkylamines.

(3) Primary and secondary amines combine with many inorganic and organic acid anhydrides—*e.g.* sulphur trioxide, acetic anhydride—to form amide-acids and acid amides.

(4) The behaviour of the amines towards *nitrous acid* is very characteristic. Primary amines are changed, at least in part, by this acid into their corresponding alcohols (p. 131):

$$C_2H_5NH_2 + NO{\cdot}OH = C_2H_5OH + N_2 + H_2O.$$

This reaction corresponds with the decomposition of ammonium nitrite into water and nitrogen:

$$NH_3 + NO{\cdot}OH = H_2O + N_2 + H_2O.$$

The alkylammonium nitrites which are formed as intermediates are only stable at very low temperatures (J.C.S. **105**, 1270).

In this reaction, intramolecular changes sometimes take place leading to the formation of secondary and tertiary alcohols instead of the expected primary one (Ber. **24**, 3350 : **26**, 2440 : Ann. **353**, 331 : C. 1908, I. 222).

Nitrosyl chloride and bromide react with primary amines and give rise to alkyl chlorides and bromides (comp. p. 194).

Nitrous acid converts the secondary amines into *nitroso-amines* (*nitrosamines*) (p. 201) :

$$(CH_3)_2NH + NO{\cdot}OH = \underset{\text{Nitroso-dimethylamine.}}{(CH_3)_2N{\cdot}NO} + H_2O$$

whereas the tertiary amines remain unaltered or undergo decomposition. Indeed, these reactions may be utilized in the separation of the amines, but naturally the primary amines are lost.

(5) Another procedure, resulting in a partial separation of the amines, depends on their varying behaviour towards carbon disulphide. The free bases (in aqueous, alcoholic, or ethereal solution) are digested with CS_2, when the primary and secondary amines form salts of alkyl dithiocarbaminic acid (*q.v.*), whilst the tertiary amines remain unaffected, and may be distilled off. On boiling the residue with $HgCl_2$ or $FeCl_3$, a part of the primary amine is expelled from the compound as mustard oil (A. W. Hofmann, Ber. **8**, 105, 461 : **14**, 2754 : and **15**, 1290).

(6) A marked characteristic of the primary amines is their ability to form *carbylamines* (*q.v.*), which are easily recognized by their odour, when heated with chloroform and alkali (*A. W. Hofmann*, Ber. **3**, 767).

(7) By the action of Cl, Br, or I alone or in the presence of alkali hydroxide, primary and secondary amines yield halogenalkylamines, *e.g.* R·NHBr.

(8) Alkyl magnesium halides (p. 220) react with primary and secondary amines, generating methane and forming RNHMgI and R_2NMgI ; with tertiary amines a certain proportion of addition compounds is formed $R_3H{<}\begin{smallmatrix}\text{Alk}\\ \text{MgI}\end{smallmatrix}$.

(9) *Oxidation* produces varying results. Alkaline permanganate easily attacks all the amines ; acid permanganate is less active, but still oxidizes with a velocity of reaction varying according to the structure of the amines, and produces ammonia, aldehyde, carboxylic acids and other bodies (Ber. **8**, 1237 : Ann. **345**, 251).

In the presence of copper powder, oxygen acts on methylamine and ethylamine, producing formaldehyde and acetaldehyde respectively, together with ammonia (Ber. **39**, 178).

The various classes of amines can be characterized by their behaviour with hydrogen peroxide and persulphuric acid (Ber. **34**, 2499 : **36**, 701, 710).

(*a*) Primary amines, RNH_2, and persulphuric acid yield various products according as R is a primary, secondary or tertiary alkyl radical. The first stage, however, in all cases is the formation of alkylhydroxylamines RNHOH (p. 204), which are further oxidized to varying results. Alkylamines with *primary* alkyl groups yield, together with other bodies, hydroxamic acids (*q.v.*), easily detected by the red colour obtained with ferric chloride ; alkylamines containing *secondary* groups give ketoximes (p. 182), and with *tertiary* alkyl groups yield nitroso-paraffins (p. 183).

(*b*) Secondary amines R_2NH yield di-alkylhydroxylamines $R_2N{\cdot}OH$ with hydrogen peroxide.

(*c*) Tertiary amines and hydrogen peroxide produce trialkylamine oxide hydrates $R_3N(OH)_2$ (p. 205).

With hydrogen peroxide in the presence of ferrous sulphate, primary amines are converted under mild conditions into the corresponding aldehyde (Biochem. Z. **71**, 169).

(10) *Tertiary amines* form addition compounds with *acid chlorides.* Such a compound, $R_3N{<}\begin{smallmatrix}Cl\\Acyl\end{smallmatrix}$ is very labile, from which the acyl group is separated in the form of condensation products (Ber. **39**, 1631), or, when in presence of alcohols or amines, as acyl esters or acyl amides (Ber. **39**, 2135), together with the formation of trialkylamine hydrochlorides.

Cyanogen bromide also forms labile addition compounds with the trialkylamines, which immediately decompose into alkyl bromides and dialkylcyanamides, from which secondary amines can be produced. These reactions constitute a method of passing from the 33 tertiary to the secondary amines (Ber. **38**, 1438). Similarly, hypochlorous acid and trimethylamine form dimethyl chloroamine $(CH_3)_2NCl$ (comp. Ber. **38**, 2154).

Bromine and iodine also yield addition compounds with tertiary amines (Ber. **38**, 2715, 3904).

(*a*) Amines and Ammonium Bases with Saturated Alcohol Radicals

(1) *Primary Amines*

Methylamine, $CH_3{\cdot}NH_2$, b.p. −6°, occurs in *mercurialis perennis* and *annua,* in bone-oil, and in the distillate from wood. It is produced from the methyl ester of *iso*cyanic acid, by the reduction of chloropicrin, $CCl_3(NO_2)$, and hydrocyanic acid, and by the decomposition of various natural alkaloids, such as caffeine, creatine, and morphine. The best way of preparing it is by warming acetbromoamide with potassium hydroxide (p. 191), or by the action of dimethyl sulphate (p. 167) on 10 per cent. ammonia at 0° (C. 1906, II. 1711). *Preparation of pure methylamine,* free from ammonia, see J.C.S. **1931**, 1477.

Methylamine is a colourless gas, with an ammoniacal odour. Its combustibility in the air and the lack of solvent action of its aqueous solution on the oxides of cobalt, nickel, and cadmium distinguish it from ammonia. At 12° one volume of water dissolves 1150 volumes of the gas. Anhydrous lithium chloride absorbs considerable quantities of methylamine (C. 1898, II. 970), which also unites with silver chloride to form $CH_3NH_2{\cdot}AgCl$ (C. 1897, I. 1156).

Methylammonium salts : *chloride,* m.p. 210° : *picrate,* m.p. 207°, dissolves with difficulty : *nitrite,* from the hydrochloride and silver nitrite, forms greenish-yellow, very deliquescent crystals, which decompose on warming into methyl alcohol, nitrogen and water (J.C.S. **99**, 1016 : **101**, 612).

Ethylamine, $C_2H{\cdot}_5NH_2$, m.p. −84°, b.p. 18° ; $D_8 = 0{\cdot}696$, is a mobile liquid, which mixes with water in all proportions (Ber. **33**, 638). It expels ammonia from ammoniacal salts, and when in excess redissolves aluminium hydroxide ; otherwise, it behaves in every respect like ammonia. Heated with potassium it becomes converted into potassium ethylamine C_2H_5NHK (C. 1897, I. 1157).

Platinichloride, m.p. 215° (dec.).

Propylamine, $C_3H_7NH_2$, b.p. 49°. *iso***Propylamine,** $C_3H_7NH_2$, b.p. 32°, occurs in white-thorn. It is prepared by reduction of acetoxime, $(CH_3)C : NOH$ (Ber. **20**, 505).

Butylamines.—n-*Butylamine,* $C_4H_9NH_2$, b.p. 76°, and iso*butylamine,* b.p. 68°.

occur in fermentation butyl alcohol. sec.-*Butylamine*, $C_2H_5CH(CH_3)NH_2$, b.p. 63°, is obtained in its dextro-rotatory form $[\alpha]_D + 7{\cdot}44°$ from the oil of *Cochlearea officinalis* (Ber. **36**, 582). tert.-*Butylamine*, b.p. 43°.

Amylamines.—n-*Amylamine*, $CH_3(CH_2)_4NH_2$, b.p. 103°, iso*amylamine*, b.p. 95°, is obtained by distilling leucine with alkalis. It occurs in numerous plants, notably among the alkaloids of ergot and tobacco (Atti. R. Accad. Lincei [5], **20**, I, 614 : Arch. exp. Path und Pharm. **61**, 113). It is soluble in water and burns with a luminous flame. Active-*amylamine*, b.p. 96°, $[\alpha]_D - 5{\cdot}86°$, is obtained from active amyl alcohol by way of amylphthalimide (method 6) (Ber. **37**, 1047). *γ-Pentylamine*, $(C_2H_5)_2CH{\cdot}NH_2$, b.p. 90°.

Hexylamine.—*γ-Amino-ββ-dimethylbutane*, $Me_3C{\cdot}CH(NH_2){\cdot}Me$, b.p. 103°, is obtained from pinacolin oxime (C. 1899, II. 474).

Heptylamine, $(C_3H_7)_2CH{\cdot}NH_2$, b.p. 130°.

Nonylamines.—n-*Nonylamine*, b.p. 195°, is difficultly soluble in water. *β-Aminononane*, $CH_3(CH_2)_7CH(NH_2)CH_3$, b.p. 69°/11 mm., from methyl heptyl ketoxime. *Di*iso*butylcarbinylamine*, $(C_4H_9)_2CH{\cdot}NH_2$, b.p. 166°, from the corresponding ketoxime.

n-**Undecylamine**, $CH_3(CH_2)_{10}NH_2$, m.p. 15°, b.p. 232°. *β-Aminoundecane*, b.p. 114°/26 mm., from methyl nonyl ketoxime (Ber. **36**, 2554).

n-**Pentadecylamine**, $CH_3(CH_2)_{14}NH_2$, m.p. 36°, b.p. 299°, from the corresponding acid chloroamide.

(2) *Secondary Amines*

The secondary amines are also designated *imine bases.*

Dimethylamine, $NH(CH_3)_2$, b.p. 7·2°, is most conveniently obtained by boiling nitrosodimethylaniline or dinitrodimethylaniline with potassium hydroxide (Ann. **222**, 119). It is a gas that dissolves readily in water. It is condensed to a liquid by the application of cold.

Diethylamine, $NH(C_2H_5)_2$, b.p. 56°, is a liquid, which is readily soluble in water ; *hydrochloride*, m.p. 76° ; *picrate*, m.p. 155°.

Di-*n*-propylamine, b.p. 110°. **Di*iso*propylamine**, b.p. 84° (Ber. **22**, R., 343).

Mixed secondary amines are produced by methods 8*a* and 8*b*. *Methylethylamine*, b.p. 35°. *Methyl*-n-*propylamine*, b.p. 63°. *Methyl*-n-*butylamine*, b.p. 91°. Methyl-*n*-heptylamine, b.p. 171° (Ber. **29**, 2110).

(3) *Tertiary Amines*

These were formerly called *nitrile bases.*

Trimethylamine, $N(CH_3)_3$, b.p. 35°, is isomeric with methylethylamine, $C_2H_5{\cdot}NH{\cdot}CH_3$, and the two propylamines, $C_3H_7{\cdot}NH_2$. It is present in herring-brine, and is produced from *betaine* (*q.v.*). It is prepared from herring-brine in large quantities, and also by the distillation of the "vinasses." It is conveniently obtained by heating ammonium chloride with formaldehyde (p. 189). Its penetrating, fish-like smell is characteristic. *Hydrochloride*, m.p. 271–275° ; *picrate*, m.p. 216°, is sparingly soluble (Ber. **29**, R. 590).

Triethylamine, $N(C_2H_5)_3$, b.p. 89°, is not very soluble in water. It is produced by heating ethyl *iso*cyanate with sodium ethoxide :

$$CO : N{\cdot}C_2H_5 + 2C_2H_5{\cdot}ONa = N(C_2H_5)_3 + CO_3Na_2.$$

(4) *Tetraalkylammonium Bases*

Whilst neither ammonium hydroxide nor mono-, di-, or tri-alkylammonium hydroxides have been prepared, yet, by the addition of the alkyl iodides to the tertiary amines, tetraalkylammonium iodides are produced ; these, when treated with moist silver oxide, yield the *alkylammonium hydroxides* :

$$N(C_2H_5)_4I + AgOH = N(C_2H_5)_4{\cdot}OH + AgI.$$

In the interaction of a methyl alcohol solution of tetramethylammonium chloride with a similar solution of potassium hydroxide, KCl is precipitated, and **tetramethylammonium hydroxide,** $(CH_3)_4NOH$, is formed. It exists as a *pentahydrate*, m.p. 63°, a *trihydrate*, m.p. 60°, and a *monohydrate*, which breaks down into trimethylamine at 130–135° (C. 1905, II. 669).

These hydroxides are perfectly analogous to those of potassium and sodium. They possess a strong alkaline reaction, saponify fats, and deliquesce in the air. They crystallize when their aqueous solutions are concentrated *in vacuo*. With the acids they yield ammonium salts, which usually crystallize well.

On exposure to strong heat they break down into tertiary amines, and alcohols or their decomposition products (C_nH_{2n} and H_2O):

$$N(C_2H_5)_4{\cdot}OH = N(C_2H_5)_3 + C_2H_4 + H_2O.$$

This reaction is of especial importance as it is frequently used to open the ring of hydrogenated cyclic bases such as pyrrolidine and piperidine, the base being submitted to "*exhaustive methylation*" and the methylammonium hydroxide being then decomposed by heat. It is frequently used for the preparation of the more unstable unsaturated hydrocarbons (*cf.* Butadiene, p. 116). Under reduced pressure, the decomposition of the alkylammonium hydroxides takes place at an appreciably lower temperature.

Tetramethylammonium iodide, $N(CH_3)_4I$, and **tetraethylammonium iodide,** $N(C_2H_5)_4I$, are prepared from iodomethane and trimethylamine, and iodoethane and triethylamine respectively; they consist of white prisms when crystallized from water or alcohol.

Other salts of the tetraalkyl ammonium bases are only obtained with difficulty from the trialkylamines by addition, although sometimes the reaction of tertiary amines with dimethyl sulphate can be used with advantage for preparing methyl sulphuric acid salts $R_3C(CH_3)OSO_3CH_3$. The *chlorides* can be obtained by the action of silver chloride on the iodides.

On heating, the tetraalkylammonium chlorides decompose into trialkylamines and alkyl chlorides, the smaller alkyl group being split off as chloride in the case of mixed tetraalkyl derivatives (Ann. **382**, 2):

$$e.g.\ NMe_2Et_2Cl \xrightarrow{\qquad} NMeEt_2 + MeCl.$$

Iodine Addition Products.—$(C_2H_5)_4NI{\cdot}I_2$, $(C_2H_5)_4NI{\cdot}2I_2$, and addition products containing even more iodine, are precipitated by iodine from the aqueous solutions of the tetraalkylammonium iodides.

Dimethyldiethylammonium iodide, $(CH_3)_2(C_2H_5)_2NI$, is obtained from dimethylamine and ethyl iodide, and from diethylamine and methyl iodide, methods of formation which should give rise to two substances having as constitutional formulæ:

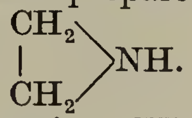
$$(CH_3)(CH_3)(C_2H_5)N{\cdot}C_2H_5I \text{ and } (C_2H_5)(C_2H_5)(CH_3)N{\cdot}CH_3I.$$

An identical product is obtained by these two methods (Ann. **180**, 173). This shows that the compounds are not "molecular compounds" but that the four alkyl groups are attached to the nitrogen atom directly. The iodine, however, is attached by an "electrovalency" as opposed to the "covalent" links by which the alkyl groups are attached. The compounds prepared by Schlenk from sodium alkyls and tetramethylammonium halides, of the type $R{\cdot}NMe_4$ are similar, in that four alkyl groups are attached by covalencies, the fifth (and only a limited number of hydrocarbon residues is capable of occupying this position), by an ionic linking. Examples of this type of compound are *triphenylmethyltetramethylammonium*, $(C_6H_5)_3C{\cdot}NMe_4$, red crystals, with a metallic lustre, hydrolysed by water into triphenylmethane and tetramethylammonium hydroxide (Ber. **49**, 603) and *benzyltetramethylammonium*, $C_6H_5CH_2{\cdot}NMe_4$, a red powder (Ber. **50**, 274). **Hydrazine** derivatives of the type $R_2N{\cdot}NMe_4$ have also been prepared (Ber. **50**, 276).

Optical resolution.—Quaternary ammonium hydroxides containing aliphatic and aromatic residues have been split into their optical isomers, but so far no base containing four aliphatic groups has been resolved. Phenylmethylethylallylammonium hydroxide $(C_6H_5)(C_3H_5)NMeEtOH$, for example, has been resolved (Ber. **32,** 3508 : **45,** 2940 : see also J.C.S. **101,** 519).

(*b*) Unsaturated Amines and Ammonium Bases

Vinylamine, $CH_2{=}CH{\cdot}NH_2$, has not yet been prepared. The previously ascribed compound is in reality ethylene imine



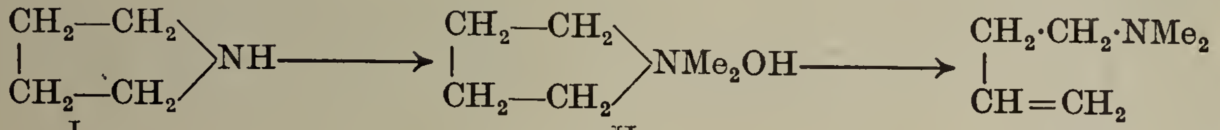
Vinyltrimethylammonium hydroxide or **neurine**, $CH_2{=}CH{\cdot}N(CH_3)_3OH$, is described after glycol with choline (*q.v.*) to which it is intimately related.

Allylamine, $CH_2{=}CH{\cdot}CH_2{\cdot}NH_2$, b.p. 58°, is best obtained from mustard oil (*q.v.*) by boiling it with 20 per cent. hydrochloric acid (Ber. **30,** 1124).

iso*Allylamine, propenylamine,* $CH_3{\cdot}CH{=}CHNH_2$, b.p. 67°, is produced by the action of potassium hydroxide on *β*-bromopropylamine (Ber. **29,** 2747).

Undecenylamine, $C_{11}H_{21}NH_2$, b.p. 239° : higher homologues, see Ber. **33,** 3580.

α-Dimethylamino-Δ^{γ}-butene, $CH_2 : CH{\cdot}CH_2{\cdot}CH_2{\cdot}NMe_2$, b.p. 95°, is obtained by the decomposition of pyrrolidine, (I) the dimethylpyrrolidinium hydroxide, (II) obtained by exhaustive methylation being submitted to distillation.



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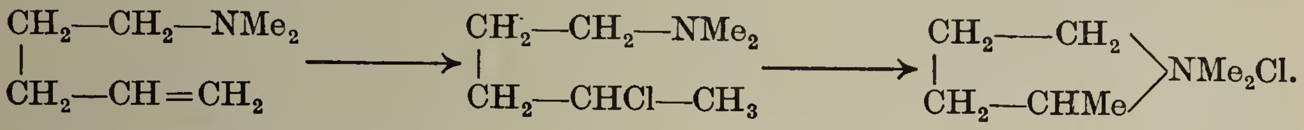
α-Dimethylamino-Δ^{δ}-pentene, $CH_2 : CH(CH_2)_3{\cdot}NMe_2$, b.p. 117°, is similarly obtained by the decomposition of piperidine. The compounds obtained by the addition of HCl to this, and to similarly constituted bases, on heating undergo isomerization with the formation of pyrrolidine derivatives (Ann. **264,** 310 : **278,** 1 : Ber. **33,** 365).



Propargylamine, $CH{\equiv}C{\cdot}CH_2NH_2$, is prepared from dibromoallylamine, $CH_2Br{\cdot}CHBr{\cdot}CH_2NH_2$, and potassium hydroxide. It is probably a gas in a free condition, but it can only be obtained in alcoholic solution or in the form of salts (Ber. **22,** 3080).

The following paragraphs, (*c*) to (*h*), deal with the *N*-substituted derivatives of the alkylamines.

(*c*) *N*-Halogen Alkylamines

These *N*-halogen derivatives may be regarded as the amides of hypochlorous and hypobromous acids. Such derivatives are produced by the action of chlorine, bromine, or iodine, alone or in the presence of alkali hydroxides, on primary and secondary amines (Ber. **8,** 1470 : **9,** 146 : **16,** 558 : **23,** R. 386 : Ann. **230,** 222), as well as by the transposition of acetodibromoamide (*q.v.*) with amines. *Dialkylchloroamines* are also obtained from tertiary bases and sodium hypochlorite, an alkyl group being eliminated (Ber. **46,** 1148).

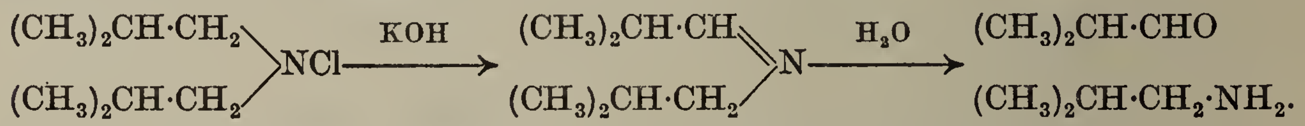
$$CH_3CH_2CH_2NH_2 \longrightarrow CH_3CH_2CH_2NHCl \longrightarrow CH_3CH_2CH_2NCl_2$$
$$(CH_3CH_2CH_2)_2NH \longrightarrow (CH_3CH_2CH_2)_2NCl.$$

When saponified they yield hypochlorous, hypobromous, and hypoiodous acids (Ber. **26,** 985).

The primary alkylamine monohalogen derivatives are less stable than the dihalogen derivatives and the secondary halogen-amines.

Methyldichloroamine, CH_3NCl_2, b.p. 58–60°, is prepared from methylammonium chloride and bleaching powder. It is a strongly smelling oil, exploding violently when heated. It forms diazomethane with hydroxylamine (p. 251 ; Ber. **28**, 1682). *Methyldiiodoamine*, CH_3NI_2, is garnet-red in colour. *Dimethyliodoamine*, $(CH_3)_2NI$, is sulphur-yellow in colour. *Ethyldichloroamine*, $C_2H_5NCl_2$, b.p. 88°, is a strongly smelling, unstable oil (Ber. **32**, 3582). *Propylchloroamine*, C_3H_7NHCl, volatilizes with decomposition. *Propyldichloroamine*, $C_3H_7NCl_2$, b.p. 117°, is a yellow oil. *Dipropylchloroamine*, $(C_3H_7)_2NCl$, b.p. 143°, etc. (Ber. **8**, 1470 : **9**, 146 : **16**, 558 : **23**, R. 386 : **26**, R. 188 : Ann. **230**, 222).

Secondary chloroamines give up hydrochloric acid in the presence of alkalis and change to the alkylimines of the aldehydes, which take up water in acid solutions forming a primary amine and an aldehyde :



$$\begin{matrix}(CH_3)_2CH\cdot CH_2\\(CH_3)_2CH\cdot CH_2\end{matrix}{>}NCl\xrightarrow{KOH}\begin{matrix}(CH_3)_2CH\cdot CH\\(CH_3)_2CH\cdot CH_2\end{matrix}{>}N\xrightarrow{H_2O}\begin{matrix}(CH_3)_2CH\cdot CHO\\(CH_3)_2CH\cdot CH_2\cdot NH_2.\end{matrix}$$

This reaction can be employed for the identification of secondary amines (C. 1897, I. 745).

Nitriles result when the dibromides of the higher primary alkylamines are treated with alkalis.

(*d*) Sulphur Derivatives of the Alkylamines

1. **Thiodialkylamines**, *thiotetraalkyldiamines*, result from the action of SCl_2 on dialkylamines in ligroin solution. *Thiodiethylamine*, $S[N(C_2H_5)_2]_2$, b.p. 87°/19 mm. (Ber. **28**, 575).

2. **Dithiotetraalkylamines**, *dithiotetraalkyldiamines*, result from the action of S_2Cl_2 on dialkylamines in ethereal solution. *Dithiodimethylamine*, $S_2[N(CH_3)_2]_2$, b.p. 82°/22 mm. *Dithiodiethylamine*, b.p. 137°/22 mm. (Ber. **28**, 166).

3. **Alkyl-thionylamines**, alkyl imides of sulphurous acid, are formed when thionyl chloride (1 mol.) acts on a primary amine (3 mols.) in ethereal solution (*Michaelis*, Ann. **274**, 187) :

$$3CH_3NH_2 + SOCl_2 = CH_3N : SO + 2CH_3NH_2\cdot HCl.$$

The members of the series with low boiling points are liquids with penetrating odour, and fume in the air. Water decomposes them into SO_2 and the primary amine. *Thionylmethylamine*, CH_3NSO, b.p. 58–59°. *Thionylethylamine*, b.p. 70–75°. *Thionylisobutylamine*, $(CH_3)_2CH\cdot CH_2\cdot N : SO$, b.p. 117°.

4. **Thionyldialkylamines**, *thionyltetraalkyldiamines*, are formed when thionyl chloride acts on the ethereal solution of the dialkylamines. *Thionyldiethylamine*, $OS[N(C_2H_5)_2]_2$, b.p. 118°/27 mm., corresponds in its composition with tetraethyl urea (Ber. **28**, 1016).

5. **Thionamic acids** are the products resulting from the interaction of sulphur dioxide and primary amines : *ethylthionamic acid*, $C_2H_5NH\cdot SO_2H$, is a white hygroscopic powder.

6. **Alkylsulphamides** and **alkylsulphaminic acids.** *Sulphamides, e.g.* $SO_2{<}\begin{smallmatrix}N(CH_3)_2\\N(CH_3)_2\end{smallmatrix}$, are formed by the action of sulphuryl chloride, SO_2Cl_2, on the free secondary amines, whereas their chlorides, $SO_2{<}\begin{smallmatrix}NR_2\\Cl\end{smallmatrix}$ result when the HCl-salts are employed. Water converts the chlorides into sulphaminic acids. $SO_2{<}\begin{smallmatrix}NR_2\\OH\end{smallmatrix}$ (Ann. **222**, 118). SO_3 reacts similarly with the primary and secondary amines, forming mono- and dialkylsulphaminic acids (Ber. **16**, 1265).

(*e*) Phosphorus Derivatives of the Secondary Alkylamines

(Ber. 29, 710)

1. **Dialkylaminochlorophosphines** are prepared by the action of phosphorus trichloride on the dialkylamines. They are liquids which give off fumes in the air, and possess an irritating odour. *Diethylaminochlorophosphine*, $(C_2H_5)_2N\cdot PCl_2$, b.p. 73°/14 mm. *Diisobutylaminochlorophosphine*, m.p. 37°, b.p. 116°/16 mm.

2. **Dialkylaminoxychlorophosphines** are obtained by the action of phosphorus oxychloride on secondary amines in aqueous solution. They are stable bodies, possessing a camphor- or pepper-like odour. *Diethylaminoxychlorophosphine*, $(C_2H_5)_2N{\cdot}POCl_2$, b.p. 100°/15 mm. *Di*-n-*propylaminoxychlorophosphine*, b.p. 170°/80 mm. *Diisobutylaminoxychlorphosphine*, m.p. 54°.

3. **Dialkylaminosulphochlorophosphines** are formed when phosphorus sulphochloride acts on dialkylamines. They can be distilled in steam, and smell like camphor. *Diethylaminosulphochlorophosphine*, $(C_2H_5)_2N{\cdot}PSCl_2$, b.p. 100°/12 mm. *Dipropylaminosulphochlorophosphine*, b.p. 133°/15 mm. *Diisobutylaminosulphochlorophosphine*, b.p. 150°/10 mm.

(*f*), (*g*), (*h*) Arsenic, Boron, and Silicon Derivatives of the Secondary Amines (Ber. 29, 714)

Diisobutylaminochloroarsine, $(C_4H_9)_2N{\cdot}AsCl_2$, b.p.$_{15}$ 125°/15 mm.

Diethylaminochloroborine, $(C_2H_5)_2N{\cdot}BCl_2$, b.p. 142°. Fumes strongly in air. *Dipropylaminochloroborine*, b.p. 99°/45 mm. *Diisobutylaminochloroborine*, b.p. 93°/17 mm.

Diethylaminochlorosilicane, $(C_2H_5)_2N{\cdot}SiCl_3$, b.p. 104°/80 mm. *Diisobutylaminochlorosilicane*, b.p. 122°/30 mm.

The chloroarsines, chloroborines, and chlorosilicanes of the secondary bases are prepared in the same way as the chlorophosphines from the corresponding chlorides.

(*i*) Nitroso-amines

All basic secondary amines (imines), like $(CH_3)_2NH$ and $(C_2H_5)_2NH$, can be converted into nitroso-amines (nitrosamines) by the replacement of the hydrogen of the imino group. They are obtained from the free imines by the action of nitrous acid on their aqueous, ethereal, or glacial acetic acid solutions, or by warming their salts in aqueous or acid solution with potassium nitrite (p. 195) (Ber. **9**, 111). They are mostly oily, yellow liquids, insoluble in water, and may be distilled without decomposition. Alkalis and acids are usually without effect upon them; with phenol and sulphuric acid they give the nitroso-reaction (*Liebermann*). When reduced in alcoholic solution by means of zinc dust and acetic acid they become converted into hydrazines (p. 202). Boiling hydrochloric acid decomposes them into nitrous acid and dialkylamines: in the presence of ferrous chloride, nitric oxide is quantitatively evolved according to the equation:

$$RR'N{\cdot}NO + FeCl_2 + HCl \longrightarrow RR'NH + FeCl_3 + NO.$$

By measurement of the evolved nitric oxide, nitroso groups can be quantitatively estimated (Ber. **60**, 1910).

Dimethylnitrosamine, $(CH_3)_2N{\cdot}NO$, b.p. 148°.
Diethylnitrosamine, $(C_2H_5)_2N{\cdot}NO$, b.p. 177°.

(*k*) Nitramines

These are produced by the action of concentrated nitric acid on various amide derivatives of the primary amines, *e.g.* their urethanes or oxamides, from which the free mono-alkyl nitramines may be obtained by means of ammonia (Ber. **18**, R. 146: **22**, R. 295: C. 1898, I. 373):

$$CH_3NHCO_2CH_3 \longrightarrow CH_3N(NO_2)CO_2CH_3 \longrightarrow \begin{array}{l}CH_3NH{\cdot}NO_2\\ \text{or } CH_3N:NOOH.\end{array}$$

One hydrogen atom in the monoalkyl nitramine molecule is replaceable by an alkali metal. As in the alkali salts of the nitroparaffins (p. 179) the metal is united to an oxygen atom forming a compound of the type RN : NOO*M*. By the reaction of the potassium alkyl nitramines with the alkyl halides, there are produced the corresponding dialkyl nitramines, which yield *unsym.*-dialkylhydrazines by reduction with zinc dust and acetic acid.

Methylnitramine, $CH_3NH{\cdot}NO_2$, m.p. 38°. *Ethylnitramine*, m.p. 3°. Potassium ethyl nitramine and iodomethane yield *N*-methylethylnitramine (see below). *Propylnitramine*, b.p. 128°/40 mm. O-*Methylethyl*isonitr*amine*, $C_2H_5{\cdot}N$:

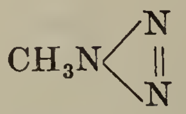
NO_2CH_3, b.p. 37°/20 mm. (C. 1898, I. 374), is prepared from silver ethyl nitramine. Butylnitramine, see Ber. **28**, R. 1058.

N-**Dialkyl nitramines** : *Dimethylnitramine*, $(CH_3)_2N{\cdot}NO_2$, m.p. 58°, b.p. 187°, is produced, together with an isomer, b.p. 112°, by the distillation of monomethylnitramine (Ber. **29**, R. 910), as well as upon treating dimethylamine and nitric acid with acetic anhydride (Ber. **28**, 402), and with diazomethane (Ber. **30**, 646). *Diethylnitramine*, b.p. 206°. *Dipropylnitramine*, b.p. 77°/10 mm.

Methylethylnitramine, b.p. 190°. *Methylpropylnitramine*, b.p. 115°/40 mm. *Methylbutylnitramine*, m.p. + 0·5° (Ber. **29**, R. 424). *Methylallylnitramine*, b.p. 95°/18 mm., is obtained, together with an *isomer*, b.p. 51°/18 mm., by the interaction of potassium methylnitramine and allyl bromide.

In the following sections are described the alkyl derivatives of hydrazine, the aliphatic diazo compounds and hydroxylamine derivatives. The corresponding *aromatic* compounds are much better known and easier to prepare, and are of greater importance in the development of organic chemistry.

Some examples of analogously constituted compounds are given below :

Methylhydrazine . .	$CH_3NH{\cdot}NH_2$	$C_6H_5{\cdot}NH{\cdot}NH_2$	Phenylhydrazine.
Potassium diazomethane	$CH_3N : NOK$	$C_6H_5N : NOK$	Potassium diazobenzene.
Methyl azide . . .			Phenyldiazoimide.
Diazoaminomethane .	$CH_3N : N{\cdot}NHCH_3$	$C_6H_5N : N{\cdot}NC_6H_5$	Diazoaminobenzene.

(*l*) Alkylhydrazines *

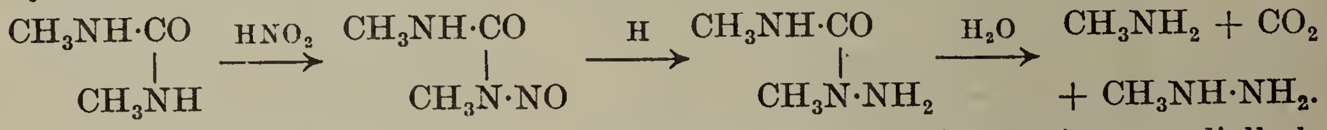
Just as the amines are derived from ammonia, so the hydrazines are derived from hydrazine or diamide, $H_2N{\cdot}NH_2$.

(1) If iodomethane acts on a cold aqueous solution of hydrazine, there are formed monomethylhydrazine and *unsym.*-dimethylhydrazine ; with an excess of iodomethane in the presence of alkalis, the final product is trimethylhydrazonium iodide (Ber. **31**, 56) :

$$NH_2{\cdot}NH_2 \xrightarrow{CH_3I} NH_2{\cdot}NHCH_3 \xrightarrow{CH_3I} NH_2{\cdot}N(CH_3)_2 \xrightarrow{CH_3I} NH_2{\cdot}N(CH_3)_3I.$$

Monoalkylhydrazines also result by the heating of salts of alkyl sulphuric acid with an aqueous solution of hydrazine (Ber. **34**, 3268).

(2) Mono-alkyl and *sym.*-dialkyl-ureas, acted on by nitrous acid, give rise to nitroso-compounds which yield alkylsemicarbazides on reduction. These are decomposed by boiling with alkalis or acids into alkylamines CO_2 and monoalkylhydrazines :



$$\begin{array}{c}CH_3NH{\cdot}CO\\ |\\ CH_3NH\end{array} \xrightarrow{HNO_2} \begin{array}{c}CH_3NH{\cdot}CO\\ |\\ CH_3N{\cdot}NO\end{array} \xrightarrow{H} \begin{array}{c}CH_3NH{\cdot}CO\\ |\\ CH_3N{\cdot}NH_2\end{array} \xrightarrow{H_2O} \begin{array}{c}CH_3NH_2 + CO_2\\ + CH_3NH{\cdot}NH_2.\end{array}$$

(3) as-*Dialkylhydrazines* are obtained from dialkylnitrosamines or dialkylnitramines by reduction with zinc and acetic acid (Ber. **29**, R. 424).

$$(CH_3)_2N{\cdot}NO + 4H = (CH_3)_2N{\cdot}NH_2 + H_2O.$$

Monoalkylhydrazines are also obtained by reduction of the monoalkylnitramines (p. 201).

(4) sym.-*Dialkylhydrazines* are formed by the action of alkyl iodides on the lead or potassium salts of diformyl hydrazine, $CHO{\cdot}NH{\cdot}NH{\cdot}CHO$, and the subsequent hydrolysis of the diformyl compound (Ber. **27**, 2279 : **31**, 62 : **39**, 3261).

They are also formed by heating pyrazole or pyrazolone (Vol. II) with alkyl

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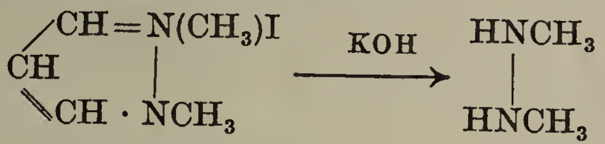
* *H. Wieland*, Die Hydrazine, Stuttgart, 1913 (Enke).

iodides and decomposing the resulting alkylpyrazole alkyl iodide with aqueous potassium hydroxide (Ber. **39**, 3257, 3267):



The mono-alkylhydrazines reduce Fehling's solution in the cold, and the dialkyl hydrazines when warmed. This behaviour differentiates them from the amines, which they otherwise resemble closely.

Methylhydrazine, $CH_3{\cdot}NH{\cdot}NH_2$, b.p. 87°, is a very mobile liquid. Its odour is like that of methylamine. It absorbs moisture and fumes in the air (Ber. **22**, R. 670. *Preparation*, see Ann. **376**, 244).

Ethylhydrazine, $(C_2H_5)HN{\cdot}NH_2$, b.p. 100°. When ethylhydrazine is acted on by potassium pyrosulphate, potassium ethylhydrazinesulphonate, $C_2H_5{\cdot}NH{\cdot}NH{\cdot}SO_3K$, is formed. Mercuric oxide changes this to potassium diazoethylsulphonate, $C_2H_5{\cdot}N{=}N{\cdot}SO_3K$.

sym.-*Dimethylhydrazine*, $CH_3NH{\cdot}NHCH_3$, b.p. 81°, forms salts with mono- and di-basic acids. sym.-*Diethylhydrazine*, b.p. 85°.

unsym.-*Dimethylhydrazine*, $(CH_3)_2N{\cdot}NH_2$, b.p. 62°, and unsym.-*Diethylhydrazine*, b.p. 97°, are mobile liquids, possessing an ammoniacal odour; they are soluble in water, alcohol and ether. *Thionyldiethylhydrazine*, $(C_2H_5)_2N{\cdot}N : SO$, b.p. 73°/20 mm. (Ber. **26**, 310).

Trimethylhydrazonium iodide, $NH_2{\cdot}N(CH_3)_3I$, m.p. 235°, with decomposition, resembles tetramethylammonium iodide. Moist silver oxide liberates the strongly alkaline tetramethylhydrazonium hydroxide, $NH_2N(CH_3)_3OH$; this consists of hydroscopic crystals, which are partially decomposed on distillation into *unsym.*-dimethyl hydrazine and methyl alcohol. Heating with iodomethane breaks down the molecule into tetramethylammonium iodide, nitrogen, and hydrogen. *Tetraethylhydrazonium iodide* is prepared from diethylhydrazine and iodoethane (Ann. **199**, 318: Ber. **31**, 57).

(*m*) Nitrosoalkylhydrazines. $RN(NO){\cdot}NH_2$ and $RN(NO){\cdot}NHR$

as-*Nitrosomethylhydrazine*, colourless needles, m.p. 45°, and *nitroso*-sym.-*dimethylhydrazine*, $CH_3N(NO){\cdot}NHCH_3$, a bright yellow oil, are obtained by the action of nitrous acid on methyl- and *sym.*-dimethylhydrazine; the dimethyl derivative can also be obtained by the methylation of the monomethyl compound by methyl sulphate. They give characteristic violet and blue colours with ferric chloride (Ann. **376**, 242).

(*n*) Alkyl Azo Compounds. $R{\cdot}N : N{\cdot}R$

Azomethane, $CH_3{\cdot}N : N{\cdot}CH_3$, is produced by the oxidation of *sym.*-dimethylhydrazine by potassium dichromate. It is a colourless, explosive gas, which condenses to a pale yellow liquid, boiling at + 1·5°. On careful heating, it breaks down into ethane and nitrogen. It is readily reduced to dimethylhydrazine by sodium amalgam, or zinc dust and caustic soda, and is split into formaldehyde and methylhydrazine by acids (Ber. **42**, 2575).

(*o*) Alkyl Diazo Compounds

The diazonium salts, so readily formed in the aromatic series, have no equivalents in the aliphatic series. The open-chain analogues of potassium diazobenzene and potassium *iso*diazobenzene are known.

Potassium methyldiazotate, $CH_3N : N{\cdot}OK$, is formed by the action of concentrated potassium hydroxide solution on nitrosomethylurethane, $CH_3N(NO){\cdot}CO_2Et$. It is very unstable, and decomposes explosively with water with the formation of diazomethane (p. 251) (Ber. **35**, 897).

Sodium methylisodiazotate, $CH_3N : N{\cdot}ONa$, forms fine, matted needles. It is produced, with evolution of nitrous oxide, by the action of sodium methoxide and ethyl nitrite on *as*-nitrosomethylhydrazine. In contradistinction to potassium methyldiazotate, it is very stable in the absence of water and carbon dioxide.

The aqueous solution gives a violet colour with copper acetate. On cautious heating it is partly decomposed into diazomethane. With acids it forms nitrogen and methyl alcohol, or the methyl ester of the acid, diazomethane being an intermediate product. It yields methylnitramine on oxidation with potassium ferricyanide, and can be obtained from the nitramine by reduction in alkaline solution (Ann. **376**, 239).

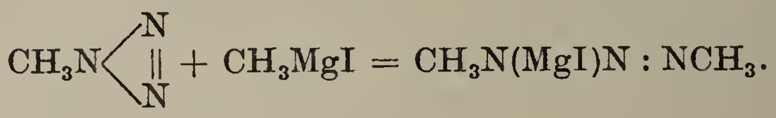
(*p*) Alkyl Diazoimides

Methyldiazoimide, methylazide, $CH_3{\cdot}N_3$, b.p. 20°, $D^{8}_{15} = 0{\cdot}869$, is the methyl ester of hydrazoic acid, and is obtained from the sodium hydrazoate NaN_3 and dimethyl sulphate in alkaline solution. It explodes violently above 500° (Ber. **38**, 1573).

Vinyl azide, $CH_2 : CH{\cdot}N_3$, b.p. 26°, is obtained from α-azido-β-iodoethane and potassium hydroxide (J.C.S. **97**, 2570).

(*q*) Diazoamino Paraffins

Diazoamino-methane, dimethyltriazene, $CH_3N : N{\cdot}NHCH_3$, m.p. − 12°, b.p. 93°, is a colourless liquid, having an odour resembling alkaloids. It is poisonous, it dissolves in water, and explodes violently on sudden heating. Its magnesium salt is produced from methyl azide and methyl magnesium iodide :



$$CH_3N\left\langle\begin{matrix}N\\ \|\\ N\end{matrix}\right. + CH_3MgI = CH_3N(MgI)N : NCH_3.$$

This substance is decomposed by water.

The *silver* derivative $CH_3N_2{\cdot}NAgCH_3$ exists as colourless needles, and the *copper* derivative $CH_3N_2{\cdot}NCu(CH_3)$ as yellow crystals (Ber. **39**, 3905). Diazoamino methane is very easily decomposed by acids, evolving nitrogen and splitting into methylamine and a methyl ester :

$$CH_3N : NHCH_3 + 2HCl = CH_3Cl + N_2CH_3NH_2{\cdot}HCl.$$

(*r*) Tetraalkyltetrazones

When mercuric oxide acts on *unsym.*-diethyl hydrazine, $(C_2H_5)_2N{\cdot}NH_2$, *tetraethyltetrazone,* $(C_2H_5)_2N{\cdot}N : N{\cdot}N(C_2H_5)_2$, is formed. This is a strongly basic liquid with an alliaceous odour.

Methylbutyltetrazone, b.p. 121°/19 mm. (Ber. **29**, R. 424).

(*s*) Alkylhydroxylamines

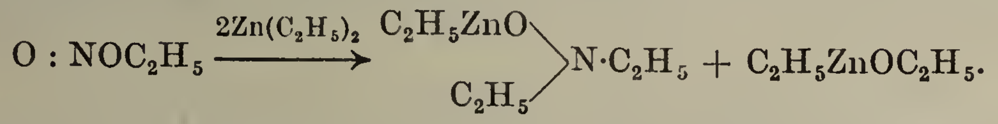
Monoalkyl hydroxylamines occur in two isomeric forms :

$NH_2{\cdot}O{\cdot}CH_3$	and	$CH_3{\cdot}NH{\cdot}OH.$
O- or α-Methyl-hydroxylamine.		*N*- or β-Methyl-hydroxylamine.

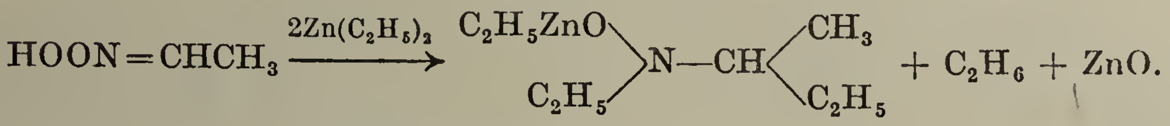
The derivatives of both varieties are obtained from the isomeric benzaldoximes (*q.v.*). The β-compounds are formed from *syn.-m.*-nitrobenzaldoxime by alkylation with sodium alcoholate and an alkyl iodide, together with the subsequent separation of the ether by means of concentrated hydrochloric acid (Ber. **23**, 599 ; **26**, 2377, 2514). α-Derivatives result from the breaking down of alkylbenzhydroxamic esters. The β-compounds are intermediate products in the reduction of the nitroparaffins with stannous chloride, or, better, with zinc dust and water (Ber. **27**, 1350), and can also be prepared by electrolytic reduction (C. 1899, II. 200). β-Alkylhydroxylamines also occur as intermediate products during the oxidation of primary amines with permonosulphuric acid, H_2SO_5, but they are mainly oxidized further to aldoximes, hydroxamic acids, ketoximes, nitroso- and nitro-compounds (p. 183).

Alkylation of hydroxylamine results essentially in the formation of β-dialkyl hydroxylamines, which in turn form the hydriodic acid salts of the trialkylamine oxides (p. 205).

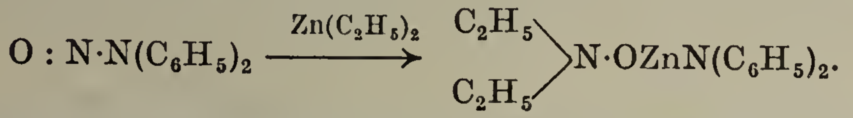
β-Dialkylhydroxylamines are also formed during the oxidation of the dialkylamines (Ber. **34**, 2499). They further result by treatment with water of the reaction products of zinc alkyls or zinc or magnesium alkyl halides on alkyl nitrites, nitroparaffins (J. pr. Chem. [2] **63**, 94, 193 : Ber. **40**, 3065) and diphenylnitrosamine (Ber. **33**, 1022). During the course of the last three reactions the following intermediate products are probably formed, if we take as examples the reaction of ethyl nitrite, nitroethane and diphenylnitrosamine with zinc ethyl:



$$O:NOC_2H_5 \xrightarrow{2Zn(C_2H_5)_2} \left.\begin{matrix}C_2H_5ZnO\\C_2H_5\end{matrix}\right> N\cdot C_2H_5 + C_2H_5ZnOC_2H_5.$$



$$HOON{=}CHCH_3 \xrightarrow{2Zn(C_2H_5)_2} \left.\begin{matrix}C_2H_5ZnO\\C_2H_5\end{matrix}\right> N{-}CH\left<\begin{matrix}CH_3\\C_2H_5\end{matrix}\right. + C_2H_6 + ZnO.$$



$$O:N\cdot N(C_6H_5)_2 \xrightarrow{Zn(C_2H_5)_2} \left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right> N\cdot OZnN(C_6H_5)_2.$$

β-Dialkylhydroxylamines are conveniently prepared by the action of nitrogen peroxide on magnesium alkyl iodides in solution in ether (Ber. **36**, 2315).

$$2NO_2 + 4C_2H_5MgI \longrightarrow 2(C_2H_5)_2NOMgI + MgO + MgI_2.$$

Reduction changes the β-dialkylhydroxylamines into dialkylamines: when sulphurous acid is employed they are converted into dialkyl sulphaminic acids (Ber. **33**, 159). See further under Trialkylamine oxides.

α-*Methylhydroxylamine, methoxylamine*, $NH_2\cdot O\cdot CH_3$, yields a *hydrochloride*, m.p. 149°. It differs from hydroxylamine in that it does not reduce alkaline copper solutions.

α-*Ethylhydroxylamine, ethoxylamine*, $NH_2\cdot O\cdot C_2H_5$, b.p. 68°.

β-*Methylhydroxylamine*, $CH_3\cdot NH\cdot OH$, m.p. 41°, b.p. 61°/16 mm. (Ber. **23**, 3597; **24**, 3528: **25**, 1716: **26**, 2514).

β-*Ethylhydroxylamine*, m.p. 59°. β-*Diethylhydroxylamine*, $(C_2H_5)_2N\cdot OH$, b.p. 76°/36 mm. β-*Dipropylhydroxylamine*, $(C_3H_7)_2N\cdot OH$, m.p. 29°, b.p. 150°.

Ethyl-sec.-*butylhydroxylamine*, $C_2H_5N(OH)CH\cdot(CH_3)\cdot C_2H_5$, b.p. 155°, prepared from nitroethane and zinc ethyl, was previously thought to be triethylamine oxide (C. 1901, I. 1146: II. 185).

αβ-*Diethylhydroxylamine*, $C_2H_5NHOC_2H_5$, b.p. 83°, and *triethylhydroxylamine*, $(C_2H_5)_2NOC_2H_5$, b.p. 98°, are formed by the action of C_2H_5Br on ethoxylamine (Ber. **22**, R. 590).

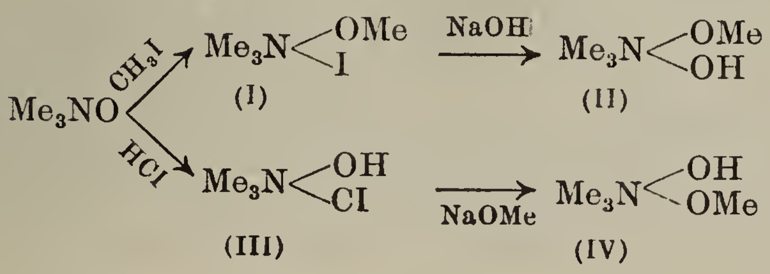
(*t*) Trialkylamine Oxides. R_3NO

These compounds are obtained in the form of their hydrates, $R_3N(OH)_2$, by the oxidation of the tertiary amines with hydrogen peroxide. Their iodides, $R_3N(OH)I$, are obtained by the action of hydrogen iodide on hydroxylamine and the *N*-alkylhydroxylamines which are formed as intermediate compounds. The free oxides, R_3NO, are obtained from the hydrates by cautious heating.

Trimethylamine oxide-hydrate, $Me_3N(OH)_2$, m.p. 96°: the free *oxide*, Me_3NO, sublimes at 180° and melts at 208° (Ann. **397**, 286). It decomposes on heating into dimethylamine and formaldehyde. *Tripropylamine oxide-hydrate*, on the other hand, breaks down on heating into propylene and *NN*-dipropylhydroxylamine (Ber. **34**, 2501).

The trialkylamine oxides combine with halogen acids to form salts of the type $R_2N(OH)X\cdot$. Alkyl iodides also combine with the trialkylamine oxides, and Meisenheimer (Ann. **397**, 273: **399**, 271) has used this reaction to support the view that the two valencies between the oxygen and nitrogen are dissimilar.

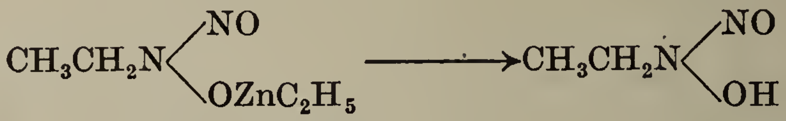
The compound (I) obtained from methyl iodide and trimethylamine oxide is converted by alkali into the free base (II). The compound (III) formed by the addition of hydrogen chloride to the oxide is treated with sodium methoxide, yielding (IV). If the two nitrogen valencies were equivalent, these compounds (II) and (IV) should be identical, whereas they are totally different (Ann. **397**, 276).



The trialkylamine oxides with three different alkyl groups, such as methylethylaniline oxide, can be split into their optically active components (Ber. **41**, 3966: Ann. **385**, 117: **428**, 252: **449**, 188). (See also stereochemistry of nitrogen, p. 45).

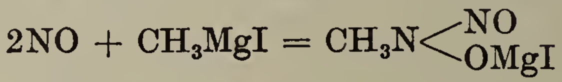
(*u*) Nitroso-*β*-alkylhydroxylamines

A member of this class of bodies was probably discovered by *Frankland*, and described under the name of *dinitroethylic acid.* It is prepared by the action of NO on zinc ethyl and the subsequent decomposition by water of the addition compound formed, and is designated as *nitroso-β-ethylhydroxylamine* (Ber. **33**, 1024):



$$CH_3CH_2N\begin{cases}NO\\OZnC_2H_5\end{cases} \longrightarrow CH_3CH_2N\begin{cases}NO\\OH\end{cases}$$

Similarly a salt of *nitroso-β-methylhydroxylamine* is prepared from NO—which reacts according to the constitutional formula O : N—N : O—and magnesium methyl iodide in solution in ether:



$$2NO + CH_3MgI = CH_3N\begin{cases}NO\\OMgI\end{cases}$$

which gives the Liebermann nitroso-reaction, and yields a well-crystallized *copper* salt, $(CH_3N_2O_2)_2Cu + \frac{1}{2}H_2O$.

6. PHOSPHORUS DERIVATIVES OF THE ALCOHOL RADICALS

A. PHOSPHINES AND ALKYL PHOSPHONIUM COMPOUNDS

Hydrogen phosphide, PH_3, has slight basic properties. It unites with HI to form phosphonium iodide, which is resolved again by water into its components. The *phosphorus bases* or *phosphines*, obtained by the replacement of the hydrogen of PH_3 by alkyls, have more of the basic character of ammonia and approach the amines in this respect. The basic character increases with the number of alkyl groups.

Thénard (1846) discovered the tertiary phosphines, and *A. W. Hofmann* (1871) first prepared the primary and secondary phosphines (Ber. **4**, 430).

Formation.—(1) By the reaction between alkyl iodides and phosphonium iodide for six hours in the presence of certain metallic oxides, chiefly zinc oxide, at 150°. The product, in the case of ethyl iodide, is a mixture of $P(C_2H_5)H_2{\cdot}HI$ and $P(C_2H_5)_2H{\cdot}HI$, the first of which is decomposed by water. The HI-salt of the diethylphosphine is not affected, but by boiling the latter with sodium hydroxide, diethylphosphine is set free (A. W. Hofmann):

$$2PH_4I + 2C_2H_5I + ZnO = 2[P(C_2H_5)H_2{\cdot}HI] + ZnI_2 + H_2O.$$
$$PH_4I + 2C_2H_5I + ZnO = P(C_2H_5)_2H{\cdot}HI + ZnI_2 + H_2O.$$
$$P(C_2H_5)H_2HI \xrightarrow{H_2O} P(C_2H_5)H_2 + HI.$$

(2) Tertiary phosphines and quaternary phosphonium iodides are produced by heating phosphonium iodide with alkyl iodides (methyl iodide) to 150–180° without the addition of metallic oxides. They can be separated by means of potassium hydroxide:

$$PH_4I + 3CH_3I = P(CH_3)_3{\cdot}HI + 3HI.$$
$$P(CH_3)_3HI + CH_3I = P(CH_3)_4{\cdot}I + HI.$$

(3) Tertiary phosphines result when alkyl halides act on calcium phosphide (*Thénard*), and (4) in the action of zinc alkyls on phosphorus chloride:

$$2PCl_3 + 3Zn(CH_3)_2 = 2P(CH_3)_3 + 3ZnCl_2.$$

(Compare the action of mercury alkyls on PCl_3, p. 208.)

(4) Primary phosphines are also obtained by heating monoalkyl phosphinic acids (p. 208).

(5) Phosphines with different alkyl groups are formed by the action of the alkylchlorophosphines (p. 208) on Grignard reagents (Ann. **449**, 213).

$$R{\cdot}PCl_2 + 2MgR'Br \longrightarrow R{\cdot}PR'_2 + MgBr_2 + MgCl_2.$$

Properties and Reactions.—The phosphines are colourless, strongly refracting, extremely powerful-smelling, volatile liquids. They are scarcely soluble in water, but dissolve readily in alcohol and ether. They oxidize very readily and have a neutral reaction.

(1) They are oxidized very energetically on exposure to the atmosphere, usually with spontaneous ignition ; hence they must be prepared in the absence of air. Moderate oxidation with nitric acid converts the primary phosphines into alkylphosphonic acids, the secondary phosphines into alkylphosphinic acids, whilst the tertiary phosphines, in the presence of air, pass into alkylphosphinic oxides :

Ethyl phosphine: $C_2H_5PH_2 \rightarrow C_2H_5PO(OH)_2$—Ethyl phosphonic acid.
Diethyl phosphine: $(C_2H_5)_2PH \rightarrow (C_2H_5)_2PO(OH)$—Diethyl phosphinic acid.
Triethyl phosphine: $(C_2H_5)_3P \rightarrow (C_2H_5)_3PO$—Triethyl phosphine oxide.

(2) They combine readily with sulphur and carbon disulphide (Ber. **25**, 2436) ; also with the halogens.

(3) The primary phosphines are, like PH_3, feeble bases. Their salts, such as PH_4I, are decomposed by water. Potassium hydroxide is required for the decomposition of the salts of the secondary and tertiary phosphines.

(4) The tertiary phosphines combine with the alkyl iodides to form tetraalkyl phosphonium iodides. These are just as little decomposed by potassium hydroxide as the tetraalkyl ammonium iodides. Moist silver oxide liberates tetraalkyl phosphonium hydroxides from them ; these, like the tetraalkyl ammonium hydroxides, are stronger bases than the alkalis :

$$P(CH_3)_3 \xrightarrow{CH_3I} P(CH_3)_4I \xrightarrow{AgOH} (PCH_3)_4OH.$$

(1) **Primary Phosphines :**

Methylphosphine, $P(CH_3)H_2$, condenses at − 14° to a mobile liquid. *Ethylphosphine*, $P(C_2H_5)H_2$, b.p. 25°. n-*Propylphosphine*, $P(C_3H_7)H_2$, b.p. 53° (C. 1903, II, 987). iso*Propylphosphine*, $P(C_3H_7)H_2$, b.p. 41°. iso*Butylphosphine*, $P(C_4H_7)H_2$, b.p. 62°.

Fuming nitric acid oxidizes the primary phosphines to alkyl phosphonic acids ; their HI-salts are decomposed by water.

(2) **Secondary Phosphines :**

Dimethylphosphine, $P(CH_3)_2H$, b.p. 25°. *Diethylphosphine*, $P(C_2H_5)_2H$, b.p. 85°. *Diiso*propyl*phosphine*, $P(C_3H_7)_2H$, b.p. 118°. *Diisoamylphosphine*, $P(C_5H_{11})_2H$, b.p. 210–215°, is not spontaneously inflammable.

Fuming nitric acid oxidizes this class of phosphines to dialkyl phosphinic acids. Water does not decompose the HI-salts of the secondary phosphines.

(3) **Tertiary Phosphines :**

Trimethylphosphine, $P(CH_3)_3$, b.p. 40°. *Triethylphosphine*, $P(C_2H_5)_3$, b.p. 127°. Both tertiary phosphines form phosphine oxides by the absorption of oxygen (Ber. **29**, 1707). They also combine with S, Cl_2, Br_2, the halogen acids, and the alkyl halides. Carbon disulphide also combines with triethylphosphine, and the product is $P(C_2H_5)_3{\cdot}CS_2$, b.p. 95°, crystallizing in red leaflets. It is insoluble in water, and sublimes without decomposition. Its production serves for the detection of carbon disulphide.

Unsymmetrical tertiary phosphines, see Ann. **449**, 213.

According to almost all of these reactions, triethylphosphine resembles a strongly positive bivalent metal—for example, calcium. By the addition of three alkyl groups, the quinquivalent, metalloidal phosphorus atom acquires the character of a bivalent alkali-earth metal. By the further addition of an alkyl group to the phosphorus in the phosphonium group, $P(CH_3)_4$, the former acquires the properties of a univalent alkali metal. Similar conditions are to be observed with sulphur, tellurium, arsenic, and also with almost all the less positive metals.

(4) **Phosphonium Bases.**—The *tetraalkylphosphonium bases* resemble, in a very high degree, both in formation and properties, the tetraalkyl ammonium

bases. *Tetramethyl-* and *tetraethyl-phosphonium hydroxide*, $P(C_2H_5)_4 \cdot OH$, are crystalline masses which deliquesce on exposure to the air. They possess a strongly alkaline reaction. When they are heated they show the great affinity of phosphorus for oxygen, for, unlike the corresponding ammonium derivatives, they break down into a trialkylphosphine oxide and a paraffin. Thus *tetramethylphosphonium hydroxide* yields trimethylphosphine oxide and methane:

$$P(CH_3)_4 \cdot OH = P(CH_3)_3O + CH_4.$$

Tetramethyl- and *tetraethylphosphonium iodides*, $P(C_2H_5)_4I$, are white crystalline substances, which are decomposed by heat into trialkyl phosphines and alkyl iodides. Tetraethylphosphonium periodide results from the prolonged interaction of iodoethane and phosphorus at 180°. With H_2S it changes into the normal iodide (Ber. **22**, R. 348).

B. ALKYLPHOSPHONIC ACIDS

These acids result, as mentioned previously, from the moderated oxidation of the primary phosphines with nitric acid; and also by oxidation of mono-alkyl phospho-acids (see below). They are derived from unsymmetrical phosphorous acid, $HPO(OH)_2$.

Methylphosphonic acid, $CH_3PO(OH)_2$, m.p. 105°. PCl_5 converts it into the *chloride*, CH_3POCl_2, m.p. 32°, b.p. 163°. On the formation of similar chlorides from alkyl-tetrachlorophosphines, see below. *Ethylphosphonic acid*, $C_2H_5PO(OH)_2$, m.p. 44°.

The dialkyl esters of alkylphosphonic acids, *e.g. diethyl ester* of *propylphosphonic acid*, $C_3H_7PO(OC_2H_5)_2$, b.p. 87°/8·5 mm., are obtained from the addition products of *sym.*-phosphorous acid ester (p. 170) and alkyl iodides (C. 1906, II. 1640; Ber. **31**, 1048), and from the interaction of alkyl oxychlorophosphines (see below) and sodium alcoholates.

C. ALKYLPHOSPHINIC ACIDS

These are derived from hypophosphorous acid, $H_2PO(OH)$.

(1) **Mono-alkylphosphinic acids.**

The action of mercury alkyls on PCl_3 results in the formation of alkydichlorophosphines:

$$(C_2H_5)_2Hg + PCl_3 = C_2H_5HgCl + C_2H_5PCl_2.$$

Ethyldichlorophosphine, b.p. 114–117°, $D_{19} = 1 \cdot 295$. *Propyldichlorophosphine*, b.p. 140–143°, $D_{19} = 1 \cdot 177$. iso*Amyldichlorophosphine*, b.p. 180–183°, $D_{23} = 1 \cdot 102$. Water decomposes these chlorides into the corresponding alkylphosphinic acids, RPO_2H_2. They are syrupy liquids which are decomposed into alkylphosphines and alkylphosphonic acids when heated:

$$3C_5H_{11}PO_2H_2 = C_5H_{11}PH_2 + 2C_5H_{11}PO_3H_2$$

Chlorine combines with the alkyldichlorophosphines forming alkyltetrachlorophosphines, $RPCl_4$, which resemble phosphorus pentachloride. Heat causes partial dissociation into PCl_3 and alkyl chloride; SO_2 produces thionyl chloride and alkyloxychlorophosphines, $RPOCl_2$; *ethyloxychlorophosphine*, b.p. 75–80°/50 mm.; *propyloxychlorophosphine*, b.p. 88–90°/50 mm.

The alkyldichlorophosphines heated with sulphur form *alkylsulphochlorophosphines*, $RPSCl_2$; *ethylsulphochlorophosphine*, b.p. 81°/50 mm. (Ber. **32**, 1572).

(2) **Dialkylphosphinic acids** result from oxidation of secondary phosphines by fuming nitric acid. *Dimethylphosphinic acid*, $(CH_3)_2PO(OH)$, m.p. 76°, forms a paraffin-like mass, which volatilizes undecomposed. *Diethyldithiophosphinic acid*, $(C_2H_5)_2PS \cdot SH$, see Ber. **25**, 2441.

D. ALKYLPHOSPHINE OXIDES

arise (1) when the tri-alkyl phosphines are oxidized in the air, together with alkyl esters of dialkyl phosphinic acid, R_2PO_2R, and alkyl phospho acids, RPO_3R_2 (Ber. **31**, 3055), or by mercuric oxide; (2) in the decomposition of the tetraalkyl phosphonium hydroxides by heat; (3) from $POCl_3$ and magnesium alkyl haloids:

$$POCl_3 + 3RMgX = OPR_3 + 3MgXCl.$$

The trialkylphosphine oxides combine with acids similarly to the trialkylamine oxides (p. 205) (C. 1906, I. 1484). *Triethylphosphine oxide*, $P(C_2H_5)_3O$, m.p.

53°, b.p. 243°, forms, for example, $P(C_2H_5)_3Cl_2$, with haloid acids, from which sodium regenerates triethylphosphine by the aid of heat. The corresponding *triethylphosphine sulphide*, $P(C_2H_5)_3S$, m.p. 94°, is prepared from triethylphosphine and sulphur.

Methylethylphenylphosphine oxide, $C_6H_5MeEtPO$, has been split into its optical components (Ber. **44**, 356). For other optically active phosphine oxides, see Ann. **449**, 213.

7. ALKYL DERIVATIVES OF ARSENIC

The alkyl compounds of arsenic form a transition from the nitrogen and phosphorus bases to the so-called organo-metallic derivatives—*i.e.* the compounds of the alkyls with the metals (p. 217). The similarity to the amines and phosphines is observed in the existence of tertiary arsines, $As(CH_3)_3$, but these do not possess basic properties, nor do they unite with acids. They show in a marked degree the property of the tertiary phosphines, in their uniting with oxygen, sulphur, and the halogens to form compounds of the type $As(CH_3)_3X_2$, and with halogen alkyls to form quaternary arsonium compounds, $As(CH_3)_4X$. The mono-, di-, and tri-alkyl arsines, derived from AsH_3, have not played nearly as important a *rôle* in the development of organic chemistry as have the cacodyl compounds.

In 1760 *Cadet* discovered the reaction which led to the study of the organic compounds of arsenic. He distilled arsenious acid together with potassium acetate, and obtained a liquid which was subsequently named, after its discoverer, *Cadet's fuming arsenical liquid.* From 1837 to 1843 *Bunsen* carried out a series of investigations (Ann. **37**, 1 : **42**, 14 : **46**, 1), and demonstrated that the chief constituent of Cadet's liquid was "alkarsine," or cacodyl oxide, whose radical "cacodyl" Bunsen also succeeded in preparing. *Berzelius* proposed the name *cacodyl* (from κακώδης, stinking) for this very poisonous body with an extremely repulsive odour. Bunsen showed that it behaved like a compound radical. Later it was found that cacodyl was a compound of two univalent radicals—$As(CH_3)_2$, combined to a saturated molecule : $(CH_3)_2As{\cdot}As(CH_3)_2$.

Valuable contributions have been made to the chemistry of the arsenic alkyls by *Cahours* and *Riche* (Ann. **92**, 361), by *Landolt* (Ann. **92**, 370), and particularly by *Baeyer*, who discovered the monomethyl arsenic derivatives, and made clear the connection existing between the alkyl-arsenic derivatives (Ann. **107**, 257).

Arsenic alkyl compounds are obtained by the following reactions.

(1) Cacodyl oxide, or alkarsine, is produced by the distillation of potassium acetate and arsenious acid. This is a delicate test, both for arsenic and for acetic acid :

$$4CH_3{\cdot}CO_2K + As_2O_3 = [(CH_3)_2As]_2O + 2K_2CO_3 + 2CO_2.$$

(2) *Trialkylarsines* are obtained by the action of zinc alkyls on arsenic trichloride :

$$2AsCl_3 + 3Zn(CH_3)_2 = 2As(CH_3)_3 + 3ZnCl_2.$$

(3) The action of the alkyl iodides on sodium arsenide produces *trialkylarsines* together with *tetraalkyldiarsines* (ethyl cacodyl).

$$AsNa_3 + 3C_2H_5I = As(C_2H_5)_3 + 3NaI.$$

(4) The interaction of trisodium or tripotassium arsenite and alkyl iodides gives rise to the sodium salts of *alkylarsonic acids* (Ann. **249**, 147 : C. 1905, I. 860), which reaction is similar to that of the formation of alkyl sulphonic acid salts from potassium sulphite and alkyl iodides (p. 175).

$$K_3AsO_3 + CH_3I = CH_3AsO(OK)_2 + KI.$$

The alkylation can be pushed further, with the production of di- and tri-alkyl compounds.

The $\cdot AsO(OH)_2$ group can be introduced into aromatic compounds by the action of diazo-compounds on sodium arsenite (see Vol. II).

Dimethylarsenious acid is obtained by the action of methyl iodide and alkali on the methylarsenic oxide produced by the reduction of methylarsenic acid by SO_2.

Cacodyl oxide, obtained by reduction of cacodylic acid, or from arsenic direct, gives trimethylarsenic oxide, when treated with iodomethane and alkali (C. 1904, I. 80):

$$(CH_3)_2AsOH + KOH + CH_3I = (CH_3)_3AsO + KI + H_2O.$$

Monoalkyl-arsine Compounds

The formation of monomethyl arsenic chloride, $As(CH_3)Cl_2$, results from the property possessed by the derivatives of the type AsX_3, of adding two halogen atoms (Cl_2) and passing into compounds of the form AsX_5. The more chlorine atoms these bodies contain, the more readily do they split off methyl chloride. Thus $As(CH_3)Cl_4$ breaks down, at 0°, into $AsCl_3$ and CH_3Cl; and $As(CH_3)_2Cl_3$, at 50°, into $As(CH_3)Cl_2$ and CH_3Cl:

$$\begin{aligned}
&As(CH_3)_3 \xrightarrow{+\,Cl_2} As(CH_3)_3Cl_2 \xrightarrow{\quad} CH_3Cl + As(CH_3)_2Cl\\
&As(CH_3)_2Cl \xrightarrow{+\,Cl_2} As(CH_3)_2Cl_3 \xrightarrow{50^\circ} CH_3Cl + As(CH_3)Cl_2\\
&As(CH_3)Cl_2 \xrightarrow{+\,Cl_2} As(CH_3)Cl_4 \xrightarrow{0^\circ} CH_3Cl + AsCl_3.
\end{aligned}$$

These reactions are the reverse of those described (method No. 4) for the progressive elaboration of methyl-arsenic compounds from arsenic.

Methyldichloroarsine, CH_3AsCl_2, b.p. 133°, results from cacodyl trichloride, $(CH_3)_2AsCl_3$ (see above), or cacodylic acid by the action of HCl, also from methylarsenic acid (see below) and an excess of PCl_3 (C. 1906, II. 101). It is a heavy, water-soluble liquid. It was used in gas-warfare. Large-scale preparation, see J. Ind. Eng. Chem. **11**, 105. *Methyldiiodoarsine*, CH_3AsI_2, is similarly obtained from methylarsenic acid by reduction by SO_2, followed by precipitation with HI. The methylarsine dihalide yields *methylarsenoxide*, CH_3AsO, m.p. 95°, by the action of Na_2CO_3; with H_2S is formed *methylarsine sulphide*, CH_3AsS, m.p. 110°; and with Ag_2O the silver salt of methylarsenic acid is obtained.

Methylarsenic acid, $CH_3AsO(OH)_2$, m.p. 161°, and *ethylarsenic acid*, $C_2H_5AsO(OH)_2$, are best prepared from potassium arsenite and alkyl iodides in aqueous solution (see above); boiling magnesia mixture precipitates the magnesium salt (C. 1905, I. 800). The sodium salt of methylarsenic acid is employed medicinally under the name of *Arrhenal* (comp. C. 1905, I. 1699). Reduction of methyl- and ethyl-arsenic acids with hypophosphite in a sulphuric acid solution leads to the formation of *methyl-* and *ethyl-arsenic* $(CH_3As)_x$ and $(C_2H_5As)_x$ as yellow, easily-polymerizable oils (C. 1904, II. 415; 1906, I. 730).

Methylarsine, CH_3AsH_2, b.p. + 2°, and *ethylarsine*, $C_2H_5AsH_2$, b.p. 36°, result from reduction of the alkyl arsenic acids by amalgamated zinc dust, alcohol, and hydrochloric acid. They are colourless liquids of a cacodyl-like odour, very poisonous, and form salts with acids with great difficulty or not at all. Methylarsine is not spontaneously inflammable. Oxidation leads first to methyl arsenoxide and then to methylarsenic acid; alkyl iodides give rise to the alkylarsines, *e.g.* tetraalkylarsonium iodide (Ber. **34**, 3594: C. 1905, I. 799).

Dialkyl Arsine Derivatives

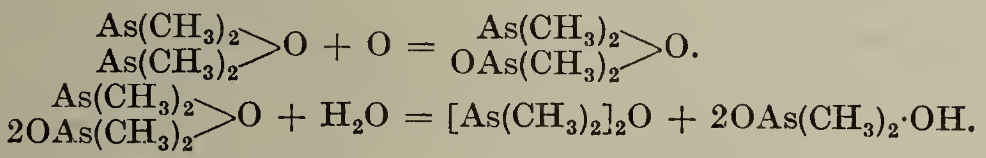
Cacodyl oxide, *alkarsine*, $[(CH_3)_2As]_2O$, m.p. − 25°, b.p. 120°, $D_{15} = 1{\cdot}462$, is the parent substance for the preparation of the dimethyl arsenic compounds. Its formation from potassium acetate and arsenic trioxide has already been given on p. 209. The crude oxide ignites spontaneously in the air. This is due to the presence in it of a slight amount of free cacodyl. When prepared from cacodyl chloride by potassium hydroxide it does not inflame spontaneously, and consists of a liquid with a stupefying odour. It is insoluble in water, but readily soluble in alcohol and in ether.

Dimethylarsine, *cacodyl hydride,* $(CH_3)_2AsH$, b.p. 36°, $D_{29} = 1{\cdot}213$, is produced when zinc and hydrochloric acid act on cacodyl chloride in alcoholic solution. It is a colourless, mobile liquid, with the characteristic cacodyl odour, and inflames spontaneously in the air. It combines with acids to form very easily dissociated salts; the halogen acid salts decompose into hydrogen and cacodyl chloride, bromide or iodide. With alkyl iodides it forms tetraalkylarsonium iodides. It unites with sulphur, producing *cacodyl disulphide,* $[(CH_3)_2As]_2S_2$, m.p. 50°, and *cacodyl sulphide,* $[(CH_3)_2As]_2S$, b.p. 211°. Oxidation produces cacodyl, cacodyl oxide, cacodylic acid, As_2O_3, CO_2, etc., according to the degree of action (Ber. **27**, 1378 : C. 1906, I. 738).

Cacodyl chloride, $As(CH_3)_2Cl$, b.p. 100°, is formed by heating trimethylarsine dichloride, $As(CH_3)_3Cl_2$ (p. 210), and by acting on cacodyl oxide with hydrochloric acid, as well as from Cl_2 and cacodyl. It is more readily obtained by heating the mercuric chloride compound of the oxide with hydrochloric acid. It unites with chlorine to form the *trichloride,* $As(CH_3)_2Cl_3$, the decomposition of which renders possible the transition from the dimethyl compounds to the monomethyl derivatives.

Cacodyl cyanide, $As(CH_3)_2{\cdot}CN$, m.p. 36°, b.p. 140°, is formed by heating cacodyl chloride with mercuric cyanide.

Cacodylic acid, *dimethyl arsenious acid,* $(CH_3)_2AsO{\cdot}OH$, m.p. 200° (decomp.), corresponds in its composition to dimethylphosphinic acid (see p. 208). Cacodyl oxide, by slow oxidation, passes into cacodyl cacodylate, which breaks down, when distilled with water, into cacodylic oxide and cacodylic acid :



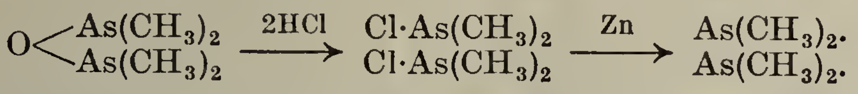
$$\begin{matrix}As(CH_3)_2\\As(CH_3)_2\end{matrix}>O + O = \begin{matrix}As(CH_3)_2\\OAs(CH_3)_2\end{matrix}>O.$$

$$2\begin{matrix}As(CH_3)_2\\OAs(CH_3)_2\end{matrix}>O + H_2O = [As(CH_3)_2]_2O + 2OAs(CH_3)_2{\cdot}OH.$$

It is also obtained by the action of mercuric oxide on cacodylic oxide. On the formation of cacodylic acid from methyl arsenoxide, KOH, and iodomethane, see method of formation 4, p. 209.

It is easily soluble in water and is colourless. Like arrhenal (p. 210) it is employed pharmaceutically, but is more poisonous. Cacodylic acid forms salts with bases KdO_2M and with acids KdOX—it is an amphoteric electrolyte (Ber. **37**, 2705, 3625, 4140). With H_2S it forms *cacodyl sulphide,* with HI *cacodyl iodide,* $(CH_3)_2AsI$. PCl_5 changes it to *dimethylarsine trichloride,* $(CH_3)_2AsCl_3$, from which water regenerates cacodylic acid.

Cacodyl, *dimethyl arsenic,* $(CH_3)_2As{\cdot}As(CH_3)_2$, m.p. − 6°, b.p. 170°, is formed by heating the chloride with zinc filings in an atmosphere of carbon dioxide :



$$O<\begin{matrix}As(CH_3)_2\\As(CH_3)_2\end{matrix} \xrightarrow{2HCl} \begin{matrix}Cl{\cdot}As(CH_3)_2\\Cl{\cdot}As(CH_3)_2\end{matrix} \xrightarrow{Zn} \begin{matrix}As(CH_3)_2.\\As(CH_3)_2.\end{matrix}$$

It is a colourless liquid, insoluble in water. Its odour is powerful, and may induce vomiting. Cacodyl takes fire very readily in the air and burns to As_2O_3, carbon dioxide and water. It yields cacodyl chloride with chlorine, and the sulphide with sulphur. Nitric acid converts it into a nitrate, $As(CH_3)_2O{\cdot}NO_2$.

Diethylarsenic, *ethyl cacodyl,* $(C_2H_5)_2As{\cdot}As(C_2H_5)_2$, b.p. 185–190°. is formed together with triethylarsine on heating sodium arsenide with ethyl iodide. It takes fire in the air, and is converted by oxidation into diethylarsenic acid, $(C_2H_5)_2AsO{\cdot}OH$.

Di*iso*amylarsine chloride, $(C_5H_{11})_2AsCl$, is produced from *iso*amyl chloride, arsenic trichloride, and sodium in ether. With H_2S it changes to *diisoamyl-*

arsine sulphide, m.p. 30° ; with bromine water it forms *diïsoamylarsinic acid*, $(C_5H_{11})_2AsOOH$, m.p. 154° (C. 1906, I. 741). *Diïsoamylarsine*, $(C_5H_{11})_2AsH$, b.p. 150°/90 mm., results from the reduction of di*iso*amylarsinic acid ; it is not spontaneously inflammable (C. 1906, I. 74).

Tertiary Arsines

The tertiary arsines are formed by the action of the zinc alkyls on arsenic trichloride, and by heating the alkyl iodides with sodium arsenide. Cacodyl, formed simultaneously, is separated by fractional distillation.

Trimethylarsine $(CH_3)_3As$, b.p. 51° (*Prep.* C. 1920, III. 538) and *triethylarsine*, $(C_2H_5)_3As$, are liquids with a very disagreeable odour. With oxygen they yield *trimethylarsenoxide* $(CH_3)_3AsO$, and *triethylarsenoxide*, $(C_2H_5)_3AsO$. These bodies correspond to triethylamine oxide (p. 205) and triethylphosphine oxide (p. 208) ; with sulphur they yield *trimethyl-* and *triethylarsine sulphide*, $As(C_2H_5)_3S$; and with Br_2 and I_2 they form *trimethylarsine bromide*, $As(CH_3)_3Br_2$, and *triethylarsine iodide*, $As(C_2H_5)_3I_2$.

Quaternary Alkyl Arsonium Compounds

Tetraalkylarsonium iodide is obtained (1) from mono-, di-, or tri-alkyl arsine by means of alkyl iodides ; (2) from sodium arsenide, mercury arsenide, or powdered arsenic and alkyl iodides by the aid of heat (Ann. **341**, 182 : C. 1907, I, 152). *Tetramethylarsonium iodide*, $As(CH_3)_4I$, and *tetraethylarsonium iodide*, $As(C_2H_5)_4I$, m.p. of both indefinite, are stable, and are of good crystalline form. They correspond with the tetraalkyl ammonium and phosphonium iodides (pp. 197, 207). Like them they are changed by moist silver oxide into the hydrated oxides : *tetramethylarsonium hydroxide*, $As(CH_3)_4OH$, and *tetraethylarsonium hydroxide*, $As(C_2H_5)_4OH$, are crystalline deliquescent bodies, possessing a strongly alkaline reaction.

8. ALKYL DERIVATIVES OF ANTIMONY

The derivatives of antimony and the alkyls are perfectly analogous to those of arsenic, but those containing one and two alkyl groups do not exist. We are indebted to Löwig and to Landolt for our knowledge of them.

Tertiary stibines are produced like the tertiary arsines :

(1) by the action of alkyl iodides on potassium or sodium antimonides ;

(2) by the interaction of zinc alkyls and antimony trichloride.

Trimethylstibine, $Sb(CH_3)_3$, b.p. 81°, $D_{15} = 1{\cdot}523$, and *triethylstibine*, $Sb(C_2H_5)_3$, b.p. 159°, are liquids which take fire in the air, and are insoluble in water. In all their reactions they exhibit the character of a bivalent metal, such as calcium or zinc. With oxygen, sulphur, and the halogens, they combine energetically, and even decompose concentrated hydrochloric acid :

$$Sb(C_2H_5)_3 + 2HCl = Sb(C_2H_5)_3Cl_2 + H_2.$$

Triethylstibine oxide, $Sb(C_2H_5)_3O$, is soluble in water, which is also true of *Triethylstibine sulphide*, $Sb(C_2H_5)_3S$, which consists of shining crystals. Its solution behaves somewhat like a calcium sulphide solution. It precipitates sulphides from solutions of the heavy metals with the formation of salts of triethyl stibine. *Triethylstibine chloride* is also prepared from antimony pentachloride and C_2H_5MgI. The *iodide*, m.p. 70° (Ber. **37**, 320).

Quaternary stibonium compounds, prepared from tertiary stibines by the addition of alkyl iodides, are changed by moist silver oxide into *tetraalkylstibonium hydroxides*. *Tetramethyl-* and *tetraethyl-stibonium iodide*, $Sb(C_2H_5)_4I$, as well as *tetramethyl- and tetraethyl-stibonium hydroxide*, $(C_2H_5)_4SbOH$, greatly resemble the corresponding arsenic derivatives in their properties. For mercury double salts with tetraalkyl stibonium halides, see C. 1900, I. 1091.

9. ALKYL COMPOUNDS OF BISMUTH

These are closely comparable with those derived from antimony and arsenic ; but in accordance with the more metallic nature of bismuth, no compounds analogous to the stibonium or arsonium derivatives are formed.

Further, in trialkyl derivatives the alkyl groups are less intimately united with the bismuth than they are with arsenic and antimony in their corresponding derivatives.

Tertiary bismuthines result from (1) the action of alkyl iodides on potassium bismuthide; (2) the interaction of zinc alkyls and bismuth tribromide. *Trimethyl bismuth*, $Bi(CH_3)_3$, and *triethyl bismuth*, $Bi(C_2H_5)_3$, are liquids which can be distilled without decomposition under reduced pressure. They explode when heated at the ordinary pressure (Ber. **20**, 1516: **21**, 2035). Bismuth trimethide is changed by hydrochloric acid to $BiCl_3$ and methane. The tri-ethide is spontaneously inflammable. It reacts with iodine to diethyl bismuth iodide, $Bi(C_2H_5)_2I$; and reacts with mercuric chloride to form ethyl bismuth dichloride, $Bi(C_2H_5)Cl_2$:

$$Bi(C_2H_5)_3 + 2HgCl_2 = Bi(C_2H_5)Cl_2 + 2Hg(C_2H_5)Cl.$$

From the alcoholic solution of the iodide the alkalis precipitate *ethyl bismuth oxide*, $Bi(C_2H_5)O$, an amorphous, yellow powder, which takes fire readily in the air. The *nitrate*, $C_2H_5Bi(NO_3)_2$, is produced by adding silver nitrate to the iodide.

ORGANIC DERIVATIVES OF ELEMENTS OF GROUP IV

10. ALKYL DERIVATIVES OF SILICON

Silicon is the nearest analogue of carbon, to which its similarity is specially close in its derivatives with the alcohol radicals, which in many respects resemble the corresponding paraffins (Friedel, Crafts, Ladenburg, Ann. **203**, 241). As early as 1863 *Wöhler* directed attention to the analogy existing between the carbon and silicon compounds, *e.g. tetramethylsilicane*, $Si(CH_3)_4$, corresponds with *tetramethylmethane*, $C(CH_3)_4$.

The alkylsilicanes are produced, like the alkylborines, when zinc alkyls act on (1) silicon halogen compounds; (2) esters of silicic acid.

(3) Silicon tetrachloride and ethyl magnesium iodide or bromide in ether give rise to a number of bodies according to the quantity of the second reacting substance employed:

$$C_2H_5SiCl_3 \longrightarrow (C_2H_5)_2SiCl_2 \longrightarrow (C_2H_5)_3SiCl \longrightarrow (C_2H_5)_4Si.$$

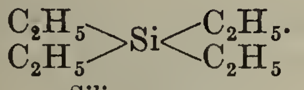
If ethyl silicon trichloride is acted on by other organo-magnesium halides, mixed alkyl silicon compounds can be obtained, *e.g.* $ClSi(C_2H_5)(C_6H_5)(C_3H_7)$ (C. 1904, I. 636: 1907, I. 1192).

(4) Silicon tetrachloride or silicon chloroform, alkyl chlorides, and sodium in ether react to form alkyl silicon compounds:

$$SiCl_4 + 4ClC_2H_5 + 8Na = Si(C_2H_5)_4 + 8NaCl.$$
$$HSiCl_3 + 3ClC_5H_{11} + 6Na = HSi(C_5H_{11})_3 + 6NaCl.$$

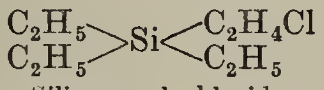
Tetramethylsilicane, *silicon tetramethyl*, $Si(CH_3)_4$, b.p. 30°, $D_0 = 0{\cdot}928$, a liquid insoluble in water, is prepared from $SiCl_4$ and zinc methyl or magnesium methyl bromide.

Tetraethylsilicane, *silicon tetraethyl*, *silicononane*, $Si(C_2H_5)_4$, b.p. 153°, $D_0 = 0{\cdot}834$, formed from $SiCl_4$ and $Zn(C_2H_5)_2$, or C_2H_5Cl and sodium, is a liquid insoluble in water. By the action of chlorine, it forms silicononyl chloride, a substitution product. Potassium acetate changes this to the acetic ester of silicononyl alcohol, which alkalis decompose into acetic acid and *silicononyl alcohol*:



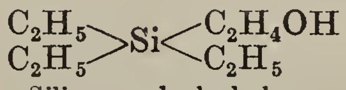
$$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\!>Si<\!\begin{matrix}C_2H_5.\\C_2H_5\end{matrix}$$

Silicononane,
b.p. 153°.



$$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\!>Si<\!\begin{matrix}C_2H_4Cl\\C_2H_5\end{matrix}$$

Silicononyl chloride,
b.p. 85°.



$$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\!>Si<\!\begin{matrix}C_2H_4OH\\C_2H_5\end{matrix}$$

Silicononyl alcohol,
b.p. 190°.

Numerous tetraalkylsilicanes have been prepared by method 3 (Ber. **44**, 2640 : **45**, 707).

Tetraisoamylsilicane, b.p. 275°. *Triisoamylsilicane*, $Si(C_5H_{11})_3H$, b.p. 245°, with bromine, passes into *triisoamylbromosilicane*, $Si(C_5H_{11})_3Br$, b.p. 279°, a heavy liquid, fuming in the air, which with ammonia gives *Triisoamylsilicol*, $Si(C_5H_{11})_3OH$, b.p. 270° (Ber. **38**, 1665).

Derivatives containing two atoms of silicon in the molecule, derived from "*disilane*," $SiH_3{\cdot}SiH_3$, are obtained by the action of magnesium alkyl halides on *disilicon hexachloride*, Si_2Cl_6, m.p. — 3°, b.p. 144°, which is obtained from 50% ferrosilicon and chlorine at 180°. *Trisilicon octachloride*, Si_3Cl_8, b.p. 210° (J.C.S. **105**, 2836).

Hexamethyldisilane, $Me_3Si{\cdot}SiMe_3$, m.p. *circa* 12°, b.p. 113°, and *hexaethyldisilane*, $Et_3Si{\cdot}SiEt_3$, b.p. 250°, are obtained from Si_2Cl_6, and the appropriate magnesium alkyl halide. They are very stable compounds, unaltered in the cold by strong acids or alkalis (Ber. **45**, 709 : **46**, 3289).

The similarity in constitution between the silicon and carbon compounds extends also to those containing oxygen, as the following compounds show.

Triethylsilicon ethoxide, $(C_2H_5)_3SiOC_2H_5$, b.p. 153°. *Diethylsilicon diethoxide* $(C_2H_5)_2Si(OC_2H_5)_2$, b.p. 155·8°. *Ethylsilicon triethoxide*, $(C_2H_5)Si(O{\cdot}C_2H_5)_3$, b.p. 159°, is a liquid with a camphor-like odour. These three compounds are produced when zinc ethyl acts on ethyl silicate, $Si(OC_2H_5)_4$ (p. 170).

Acetic anhydride converts triethylsilicon ethoxide into an acetic ester. When this is hydrolysed by potassium hydroxide, it yields *triethylsilicol*, $(C_2H_5)_3SiOH$, corresponding in constitution with triethylcarbinol.

Acetyl chloride changes diethyl silicon diethoxide into *diethylsilicon chloride*, $(C_2H_5)_2SiCl_2$, b.p. 148°. Water converts this into *diethylsilicon oxide*, $(C_2H_5)_2SiO$, corresponding with diethyl ketone in composition.

With acetyl chloride, ethylsilicon triethoxide forms *ethylsilicon trichloride*, $(C_2H_5)SiCl_3$, b.p. about 100°. This liquid fumes strongly in the air, and when treated with water passes into *ethylsilicic acid*, $(C_2H_5)SiO{\cdot}OH$ (silico-propionic acid), which is analogous to propionic acid, $C_2H_5{\cdot}CO{\cdot}OH$, in constitution. It is a white, amorphous powder, which becomes incandescent when heated in the air. It only resembles the corresponding propionic acid by being acidic in character.

By the action of ethyl alcohol and water on Si_2Cl_6 the compounds *hexaethoxydisilane*, $(EtO)_3Si{\cdot}Si(EtO)_3$, and *silico-oxalic* acid, $HOSiO{\cdot}SiOOH$, respectively are produced. The Si·Si link is destroyed in both compounds by the action of KOH, the silico-ether linkage, Si·O·Si being substituted (J.C.S. **105**, 2860).

11. ALKYL DERIVATIVES OF GERMANIUM

Germanium ethyl, $Ge(C_2H_5)_4$, b.p. 160°, is formed when zinc ethyl acts on germanium chloride. It is a liquid with a leek-like odour. (*Cl. Winkler*, J. pr. Chem. [2] **36**, 204.)

12. ALKYL DERIVATIVES OF TIN

The best-known tin-organic derivatives are those containing four alkyl groups, of the general formula SnR_4. In addition to these, further compounds are known, referable to the types SnR_2 and $R_3Sn{\cdot}SnR_3$.

The alkyl-tin derivatives have been studied by *Löwig*, *Cahours*, *Ladenburg* and others. A general account of the organic tin compounds is given in Z. anorg. Chem. **68**, 102, and Ber. **50**, 1803.

The methods used for the preparation of the tin compounds are of the same general type as those used for arsenic, antimony and other elements.

(1) Action of zinc alkyls or magnesium alkyl halides on $SnCl_2$ and $SnCl_4$: the compounds $SnMe_4$, $SnEt_4$ and $SnEt_2$ have been prepared by this method (Ber. **37**, 320 : C. 1904, I. 353).

(2) Action of alkyl iodides on tin-sodium alloys (containing tin alone or

tin + zinc). If the alloy contains little sodium, the chief product is SnR_2I_2; if the sodium content is high, the product is SnR_3I.

Diethyl tin, $Sn(C_2H_5)_2$, is a thick oil, which decomposes on heating into $Sn(C_2H_5)_4$ and tin, and which readily combines with oxygen, halogens or alkyl iodides. It is formed from tin diethyl chloride by reduction with sodium amalgam in ethereal solution, or by the action of magnesium ethyl bromide on $SnCl_2$ (Ber. **44**, 1269). *Diethyl tin chloride*, $SnEt_2Cl_2$, m.p. 85°, b.p. 220°: *diethyl tin iodide*, $SnEt_2I_2$, m.p. 44·5°, b.p. 245°. *Diethyl tin oxide*, $SnEt_2O$, forms a white insoluble powder, which is precipitated from the halogen derivatives by ammonia or other alkalis, and which dissolves in excess of alkali and forms salts, such as $SnEt_2(ONO_2)_2$ with acids.

Tetramethyl tin, $Sn(CH_3)_4$, b.p. 78°, and **tetraethyl tin**, $Sn(C_2H_5)_4$, b.p. 181°, $D_{23} = 1{\cdot}187$; both are colourless, ethereal-smelling liquids, insoluble in water. By the action of the halogens the alkyls are successively eliminated; hydrochloric acid acts similarly:

$$Sn(C_2H_5)_4 + I_2 = Sn(C_2H_5)_3I + C_2H_5I, \text{ etc.}$$
$$Sn(C_2H_5)_4 + HCl = Sn(C_2H_5)_3Cl + 2C_2H_6, \text{ etc.}$$

(For tin tetraalkyls with different alkyl groups see C. 1904, I. 353.)

The alkyl groups are not so firmly united in the tin alkyls as they are in the alkyls of silicon.

Triethyl tin chloride, $Sn(C_2H_5)_3Cl$, b.p. 208–210°, $D = 1{\cdot}428$: *triethyl tin iodide*, $Sn(C_2H_5)_3I$, b.p. 231°, $D_{22} = 1{\cdot}833$. Alcohol and ether are solvents for both. When either is acted on by silver oxide or potassium hydroxide, there is produced *triethyl tin hydroxide*, $Sn(C_2H_5)_3{\cdot}OH$, m.p. 66°, b.p. 272°, sparingly soluble in water, but readily soluble in alcohol and ether. It reacts strongly alkaline, and yields crystalline salts with the acids, *e.g.* $Sn(C_2H_5)_3{\cdot}O{\cdot}NO_2$. When the hydroxide is heated for some time to almost boiling temperature, it breaks down into water and *triethyl tin oxide*, $\begin{matrix}Sn(C_2H_5)_3\\Sn(C_2H_5)_3\end{matrix}\!\!>O$, an oily liquid, which in the presence of water at once regenerates the hydroxide.

By the action of sodium on the trialkyl tin halides, the *hexaalkyldistannanes* $H_3Sn{\cdot}SnR_3$, are produced (Ber. **59**, 1808).

Hexaethyldistannane, $(C_2H_5)_3Sn{\cdot}Sn(C_2H_5)_3$, is a heat-stable liquid, b.p. 161°/23 mm. The distannane derivatives are decomposed by atmospheric oxygen to trialkyl tin oxides, and by halogens into trialkyl tin halides.

Methylstannonic acid, CH_3SnOOH, is formed at ordinary temperatures from iodomethane and an alcoholic solution of an alkaline stannous solution similarly to the preparation of methylsulphonic acid and methylarsenic acid (pp. 175, 210) from iodoethane and an alkaline solution of sulphurous and arsenious acids:

$$ICH_3 + HSnO_2K + KOH = CH_3SnO_2K + KI + H_2O.$$

Methyl stannonic acid is a white amorphous powder, soluble in potassium hydroxide solution, from which it is precipitated by CO_2. Warming with alkalis produces stannates and *dimethylstannic oxide*, which by distillation with alkalis decomposes into stannates and *trimethylstannic hydroxide*:

$$2CH_3SnO_2K \longrightarrow SnO_3K_2 + (CH_3)_2SnO.$$
$$3(CH_3)_2SnO \xrightarrow{2KOH} 2(CH_3)_3SnOH + K_2SO_3.$$

Methyl stannonic acid is transformed by the halogen acids into *Methyl tin triiodide*, CH_3SnI_3, m.p. 86°, *methyl tin tribromide*, CH_3SnBr_3, m.p. 53°, and *methyl tin trichloride*, CH_3SnCl_3, m.p. 43°, which fume in the air like tin tetrachloride. Thus, methyl stannonic acid behaves like cacodylic acid, as an amphoteric electrolyte.

Methyl stannic triiodide can also be obtained from stannous iodide and iodomethane at 160°; from stannic iodide and magnesium methyl-iodide together with *trimethyl tin iodide*, $(CH_3)_3SnI$, b.p. 170° (Ber. **36**, 3027: **37**, 4618); and by heating together tin tetramethyl and stannic iodide (C. 1903, II. 106).

13. ALKYL DERIVATIVES OF LEAD

The lead alkyl compounds resemble the tin derivatives closely, and among the aliphatic series, the tetravalent compounds PbR_4 are far the best known. In the aromatic series, compounds $PbAr_2$ and $PbAr_3$ (where Ar = an aromatic radical) are better known (*cf.* Vol. II and Ber. 54, 2060 : 55, 888).

The compounds are formed (1) by the action of zinc ethyl or magnesium ethyl iodide on lead chloride ($PbCl_2$) whereby the tetra-alkyl derivative $PbEt_4$ is produced.

(2) By the action of alkyl iodides on lead-sodium alloy, yielding the compound Pb_2Et_6.

Tetramethyl lead, b.p. 110°, and **tetraethyl lead,** b.p. 91°/19 mm., are oily liquids which cannot be distilled undecomposed. The tetraethyl derivative has been much used recently as an " anti-knock " substance in motor-fuels.

Triethyl lead chloride, $Pb(C_2H_5)_3Cl$, and *triethyl lead iodide,* $Pb(C_2H_5)_3I$, are formed from tetraethyl lead and triethyl lead by hydrochloric acid or iodine respectively. The iodide is transformed by moist silver oxide into a thick, strongly alkaline liquid, dissolving with difficulty in water and forming salts with acids. *Triethyl lead sulphate,* $[Pb(C_2H_5)_3]_2SO_4$, is slightly soluble in water.

The triethyl halides form the starting substance for the preparation of mixed tetraalkyl derivatives, PbR'_3R. (Ber. **50**, 202).

By the action of halogens on the tetraalkyl derivatives at − 20°, two alkyl groups are split off with the formation of compounds PbR_2X_2, which react with the Grignard compounds to give another series of mixed lead tetraalkyls of the type PbR'_2R_2 (Ber. **49**, 1546).

The compound Pb_2Et_6 has also been prepared by the electrolysis of $PbEt_3OH$ in ethyl alcohol. It is a heavy yellow oil, unstable in air (J.A.C.S. **45**, 1821).

ORGANIC DERIVATIVES OF THE ELEMENTS OF GROUP III

14. ALKYL DERIVATIVES OF BORON

These are formed by the action of zinc alkyls on (1) boron trichloride, (2) ethyl borate (p. 169) (*Frankland*, Ann. **124**, 129) :

$$2B(OC_2H_5)_3 + 3Zn(C_2H_5)_2 = 2B(C_2H_5)_3 + 3(C_2H_5{\cdot}O)_2Zn.$$

Trimethylborine is a gas. *Triethylborine*, $B(C_2H_5)_3$, b.p. 95°. Both ignite in contact with the air and possess an extremely penetrating odour. When heated together with hydrochloric acid, triethylborine decomposes into diethylborine chloride and ethane :

$$B(C_2H_5)_3 + HCl = B(C_2H_5)_2Cl + C_2H_6.$$

Slowly oxidized in the air, triethylborine passes into the *ester,* $B(C_2H_5)(O{\cdot}C_2H_5)_2$, b.p. 125°, which water decomposes into *ethylboric acid,* $C_2H_5{\cdot}B(OH)_2$. For other alkylboric acids, see Ber. **42**, 3095.

15. ALKYL DERIVATIVES OF ALUMINIUM

The aluminium alkyl derivatives resemble those of boron. They are obtained by the action of mercury alkyls on aluminium or by adding anhydrous aluminium chloride to an ethereal solution of a Grignard reagent (Ber. **56**, 466). Aluminium alkyl derivatives are also obtained by the direct action of alkyl bromides on clean turnings of a magnesium-aluminium alloy (Electrometal) (Ber. **56**, 466).

Trimethyl aluminium, $Al(CH_3)_3$, b.p. 130°. *Triethyl aluminium,* $Al(C_2H_5)_3$, b.p. 194°. Both are colourless liquids and are spontaneously inflammable. Water decomposes them with great violence, forming methane (or ethane) and aluminium hydroxide. Their vapour densities indicate a mono- rather than a di- molecular constitution (see Ber. **22**, 551 ; Z. physik. Chem. **3**, 164).

16. ALKYL DERIVATIVES OF THALLIUM

Thallium dialkyl halides of the type TlR_2X are prepared by the interaction of thallium chloride, $TlCl_3$, and magnesium alkyl halides in ether solution (p. 219). They are crystalline bodies, dissolving in water with great difficulty, and decomposing on being heated. They can be recrystallized from an alkaline aqueous solution without decomposition ; moist silver oxide produces strongly alkaline, easily soluble hydroxides, *e.g. diethyl thallium hydroxide*, $Tl(C_2H_5)_2OH$, which absorb CO_2 from the atmosphere and precipitate hydroxides from solutions of the metals, thus resembling thallous hydroxide TlOH (Ber. **37**, 2051).

Triethyl thallium, $TlEt_3$, from $TlEt_2Cl$ and LiEt, b.p. 54·6°/1·5 mm. (J.A.C.S. **52**, 2999).

ORGANIC DERIVATIVES OF THE ELEMENTS OF GROUP II

ORGANOMETALLIC COMPOUNDS

Although some of the compounds which have already been discussed really belong to the class of "*organometallic compounds*," it is to the compounds formed by the elements of Groups I and II of the periodic table that this description is most usually applied.

The metallo-organic compounds are those resulting from the union of metals with univalent alkyls ; those with the bivalent alkylenes, C_nH_{2n}, have not yet been prepared. Inasmuch as we have no marked line of difference between metals and non-metals, the metallo-organic derivatives are connected, in the one direction, through the derivatives of antimony and arsenic, with phosphorus and nitrogen bases ; and in the other, through the selenium and tellurium compounds, with the alkyl sulphides and ethers ; whereas the lead derivatives approach those of tin, and the latter the silicon alkyls and the hydrocarbons.

Within recent years, in addition to the derivatives of zinc, cadmium, mercury and magnesium, which have been known the longest, derivatives of practically every metal, including even the alkali metals, have been prepared.

Those compounds in which the metals present their maximum valence, *e.g.* :

$$\overset{\text{II}}{\mathrm{Hg}}(CH_3)_2 \qquad \overset{\text{III}}{\mathrm{Al}}(CH_3)_3 \qquad \overset{\text{IV}}{\mathrm{Sn}}(CH_3)_4 \qquad \overset{\text{IV}}{\mathrm{Pb}}(CH_3)_4$$

are volatile liquids, usually distilling without decomposition in vapour form ; therefore, the determination of their vapour density is an accurate means of establishing their molecular weight, and the valence of the metals.

The behaviour of the metallo-organic radicals, derived from the molecules by the loss of single alkyl groups, is especially noteworthy. The univalent radicals, *e.g.* :

$$—\overset{\text{II}}{\mathrm{Hg}}(CH_3) \quad —\overset{\text{III}}{\mathrm{Tl}}(CH_3)_2 \quad —\overset{\text{IV}}{\mathrm{Sn}}(CH_3)_3 \quad —\overset{\text{IV}}{\mathrm{Pb}}(CH_3)_3 \quad —\overset{\text{V}}{\mathrm{Sb}}(CH_3)_4,$$

show great resemblance to the alkali metals in all their derivatives. Like other univalent radicals, they cannot be isolated. They yield hydroxides, *e.g.* :

$$Hg(C_2H_5)·OH \qquad Tl(CH_3)_2·OH \qquad Sn(CH_3)_3·OH,$$

which are comparable to KOH and NaOH. Some of the univalent radicals, when set free from their compounds, become doubled:

$$\begin{array}{c} As(CH_3)_2 \\ | \\ As(CH_3)_2 \end{array} \qquad \begin{array}{c} Si(CH_3)_3 \\ | \\ Si(CH_3)_3 \end{array} \qquad \begin{array}{c} Sn(CH_3)_3 \\ | \\ Sn(CH_3)_3 \end{array} \qquad \begin{array}{c} Pb(CH_3)_3 \\ | \\ Pb(CH_3)_3. \end{array}$$

By the loss of two alkyls from the saturated compounds, the divalent radicals result:

$$=\overset{III}{Bi}(CH_3) \qquad =\overset{IV}{Te}(CH_3)_2 \qquad =\overset{IV}{Sn}(C_2H_5)_2 \qquad =\overset{V}{Sb}(CH_3)_3.$$

In their compounds (oxides and salts) these resemble the divalent alkali earth metals, or the metals of the zinc group. A few of them can be obtained in the free condition. As unsaturated molecules, however, they show strong inclination to saturate two single affinities directly. Antimony triethyl, $Sb(C_2H_5)_3$ (see p. 212), has the power of reacting with acids to form salts, liberating hydrogen at the same time.

Finally, the trivalent radicals, like $\equiv As(CH_3)_2$, can also figure as univalent, as in the case of vinyl, C_2H_3. These may be compared to aluminium; and cacodylic acid, $As(CH_3)_2O{\cdot}OH$ (p. 211), to aluminium metahydroxide, $AlO{\cdot}OH$.

We conclude, therefore, that the electro-negative metals, by the successive union of alcohol radicals, always acquire a more strongly basic, alkaline character. This also finds expression with the non-metals (sulphur, phosphorus, arsenic, etc.). (Comp. pp. 173, 208, 212.)

The first metallo-organic derivatives were prepared by *Frankland.* The *zinc alkyls* are particularly important as alkylating bodies, but are being replaced by *magnesium alkyl halides,* which are much more convenient to work with.

Methods of Formation:

(1) Action of metals (Mg, Zn, Hg) on alkyl iodides.

(2) Action of alloys (Pb, Na) on alkyl iodides (see Bi-, Sb-, Sn-compounds).

(3) Action of metals (K, Na, Be, Al) on metallo-organic bodies (zinc alkyls, mercury alkyls).

(4) Action of metallic chlorides ($PbCl_2$) on metallo-organic derivatives (zinc alkyls or magnesium alkyl halides; comp. BCl_3, $SiCl_4$, $SnCl_4$, $GeCl_4$ on zinc alkyls or magnesium alkyl halides).

(5) By the action of aluminium carbide on the hydrochloric acid solutions of metallic salts (Ber. **46,** 3738).

17. ALKYL DERIVATIVES OF BERYLLIUM

Diethyl beryllium, $Be(C_2H_5)_2$, b.p. 185–188°, is prepared from the metal and zinc ethyl. It is spontaneously inflammable. *Dipropyl beryllium,* $Be(C_3H_7)_2$, b.p. 245° (see also Ber. **56,** 467: J.A.C.S. **45,** 2693).

18. ALKYL DERIVATIVES OF MAGNESIUM

The most important organic derivatives of magnesium are the *magnesium alkyl halides,* usually referred to as the "*Grignard*

Reagents " after the investigator who first studied their preparation and properties.* These compounds are much easier to prepare and to manipulate than the magnesium dialkyl compounds.

Magnesium dialkyls. *Dimethyl magnesium* $MgMe_2$ and the corresponding *ethyl* compound $MgEt_2$ are white solids spontaneously inflammable even in a CO_2 atmosphere. They decompose on heating with the formation of hydrocarbons, and with water react similarly to the zinc alkyls. They are prepared by the action of magnesium on the corresponding mercury derivative (Ann. **276**, 129).

Magnesium alkyl halides. Grignard Reagents.

In 1899 Barbier (Compt. rend. **128**, 110) discovered that when the product of reaction between methylheptenone, $C_6H_{11}·CO·CH_3$, and methyl iodide in the presence of magnesium and ether was treated with an acid, the compound dimethylheptenol, $C_6H_{11}·C(OH)(CH_3)_2$, could be isolated. As zinc methyl reacts with ketones to form similar products, it was thought that the action of the magnesium might be to form CH_3MgI as an intermediate product, and Grignard who subsequently investigated the reaction was able to show that the reaction was a general one and that compounds of the type MgRX were produced from alkyl halides and magnesium in the presence of ether. This reaction is now of the greatest importance in the synthesis of very many organic compounds.

The reaction proceeds most readily with the iodides and bromides : the chlorides frequently require the addition of a little iodide (*cf.* Ber. **38**, 2759), mercuric chloride (Am. Chim. Phys. [8] **9**, 533), or previously prepared Grignard solution (Ber. **39**, 1746 : Bull. Soc. Chim. [3] **35**, 1079) to start the reaction. When secondary and tertiary alkyl halides are used, the reaction sometimes takes place in a different manner, halogen hydride being split off : at low temperatures the reaction may proceed normally. The reaction takes place readily with the aromatic halogen derivatives such as iodobenzene.

The solvent, usually ether, takes a very important part in catalysing the reaction. When excess of solvent is distilled off, the magnesium alkyl halides remain behind usually as crystalline " etherates," $MgRI,Et_2O$, $MgRI,2Et_2O$. Other compounds such as tertiary amines can take the place of the ether in the reaction, compounds of the type $MgRI,NR_3$ being produced (Ber. **37**, 3088 : *Oddo*, Atti. R. Accad. Lincei. [5] **13**, II. 100). The addition of a few drops of dimethylaniline to a benzene solution of iodoethane, for example, causes the production of pure magnesium ethyl iodide in the form of a white powder by the action of magnesium. This reacts analogously to the " etherates " and dissolves in ether, with an evolution of heat, to form these bodies (Ber. **38**, 4534 : **39**, 1674). The latter compounds are not so important as those formed in the presence of ether.

The constitution of the Grignard reagent has been much studied,

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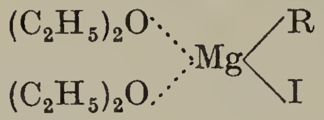
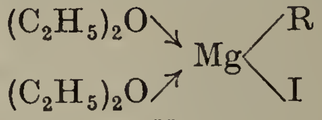
* "Sur les combinaisons organomagnésiennes mixtes et leur applications à des synthèses." Bull. soc. chim. [4], **13**, 1 : *cf.* also *Schmidt*, Über die organischen Magnesuimverbindungen und ihre Anwendung zu Synthesen, Teil I und II, Stuttgart, 1905 and 1908.

and can best be represented by the formula of Meisenheimer (I) (Ber. 54, 1655). The modern electronic representation of this is (II):



(I)



(II)

The Grignard reagents in ethereal solution are very reactive and behave similarly to the zinc alkyls. The reactions, however, usually take place more smoothly.

Reactions.—(1) The compounds are decomposed energetically by water, alcohols, ammonia, and primary and secondary amines with the formation of hydrocarbons.

$$R'MgI + ROH \longrightarrow R'H + ROMgI$$
$$R'MgI + RNH_2 \longrightarrow R'H + RHN{\cdot}MgI$$

Acetylene, hydrocyanic acid, indene (Vol. II: Compt. rend. **152,** 272) and fluorene (Vol. II: Compt. rend. **152,** 1493) behave similarly. See also pyrrole and indole (Vol. III).

This reaction is the basis of the method for the estimation of "active" hydrogen atoms (Zerewitinoff, Ber. **45,** 2384: Z. anal. Chem. **52,** 729: Ber. **47,** 1659, 2417: micromethod, see Flaschenträger, Z. physiol. Chem. **146,** 219).

The compound $MgNH_2I$ obtained by the action of dry ammonia on the ethereal solution of a Grignard reagent is very reactive and is sometimes useful for the preparation of amides from acid chlorides and esters. It reacts readily with acetonylacetone to yield 2:5-dimethylpyrrole (Gazzetta, **53,** i, 64).

(2) Oxygen and sulphur are absorbed, and alcoholates and mercaptides result:

$$RMgX + O \longrightarrow ROMgX \qquad RMgX + S \longrightarrow RSMgX.$$

(3) CO_2, COS, CS_2, SO_2, are taken up, forming salts of carboxylic acids, thiocarbonic acids, carbithionic acids, sulphinic acids, *e.g.*:

$$C_2H_5MgI + CO_2 = C_2H_5COOMgI.$$

(4) NO_2 forms salts of the β-dialkyl hydroxylamines (p. 205) and NO those of the β-nitroso-alkyl hydroxylamines (p. 206).

From alkylazoimides, diazoamino compounds (p. 204) are formed.

From aliphatic diazo-compounds, hydrazones are produced (Monatsh. **34,** 1609).

(5) From *aldehydes* and *ketones*, carboxylic esters, acid anhydrides, chlorides and salts, primary, secondary and tertiary alcohols are formed (see p. 133).

Many of these tertiary alcohols give up water, yielding olefines, especially in presence of an excess of RMgX; see *e.g.* diolefines (p. 115), etc.

Ethylene oxide and its homologues unite with the magnesium alkyl halides to form alcohols (p. 134).

Formic acid derivatives, such as esters, orthoesters, imido ethers, dialkylamides, *iso*nitriles, under suitable conditions, yield aldehydes.

Carboxylic acid amides and nitriles frequently give rise to ketones.

The magnesium alkyl halides are added on to many $\alpha\beta$-olefine ketones, carboxylic acid esters, and nitriles at the double bond, forming the corresponding β-alkyl paraffin compounds (C. 1907, I. 559, etc.).

With Schiff's bases, RCH : NR′, they form secondary amines, RR″CH·NHR′. Often these bodies, ketones, and other substances are only reduced by the organo-magnesium halides (Ber. **38**, 2716 : C. 1906, II. 312).

(6) Iodine changes the magnesium alkyl chlorides and bromides to alkyl iodides.

(7) Halogen or sulphuric acid compounds of many radicals have the haloid or sulphuric acid residues replaced by alkyl, *e.g.* :

$$C_5H_{11}MgBr + BrCH_2OCH_3 \longrightarrow C_5H_{11}CH_2OCH_3.$$
$$C_5H_{11}MgBr + SO_4(CH_3)_2 \longrightarrow C_5H_{11}{\cdot}CH_3.$$

By similar reactions for the preparation of *iso*amyl and *iso*hexyl magnesium bromides, di*iso*amyl and di*iso*hexyl are formed as by-products (Ber. **36**, 3084).

(8) The chlorides of many metals and non-metals react with the Grignard reagents to form alkyl derivatives of these elements (see under alkyl derivatives of P, As, Sb, Si, etc.).

(9) Good yields of the simpler alcohols are obtained from the Grignard reagents by the action of hydrogen peroxide (Gazzetta, **51**, ii, 343) :

$$MgRX + H_2O_2 \longrightarrow R{\cdot}OH + MgX{\cdot}OH.$$

19. ALKYL DERIVATIVES OF ZINC

Zinc methyl and zinc ethyl were discovered in 1849 by *Frankland* (Ann. **71**, 213 : **85**, 329 : **99**, 342). The zinc alkyls are exceedingly reactive, and are, on this account, a very important class of the metallic alkyls.

Methods of Formation.—(1) When zinc filings act on iodides of the alcohol radicals in sunlight, iodides are formed, which are decomposed by heat into zinc alkyls and zinc iodide :

$$C_2H_5I + Zn = IZnC_2H_5.$$
$$2Zn(C_2H_5)I = Zn(C_2H_5)_2 + ZnI_2.$$

The action may be accelerated if the zinc turnings have been previously corroded, or by the application of zinc-sodium or zinc-copper. In preparing zinc ethyl, ethyl iodide is poured over zinc cuttings and a little pure zinc ethyl is then added. The formation of $IZn{\cdot}C_2H_5$ is then completed at the ordinary temperature, and this body separates in large, transparent crystals. When it is heated in a current of CO_2, it yields zinc ethyl (Ann. **152**, 220 : Ber. **26**, R. 88 : C. 1900, II. 460). It is also formed by the solution of zinc in a boiling ether solution of iodoethane (C. 1901, II. 24).

(2) The mercury alkyls are converted by zinc into zinc alkyls, with the separation of mercury :

$$Hg(C_2H_5)_2 + Zn = Zn(C_2H_5)_2 + Hg.$$

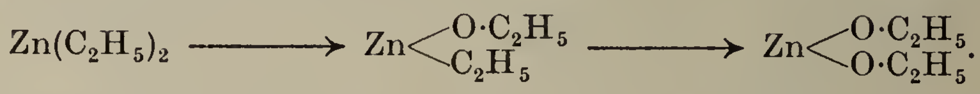
Properties.—The zinc alkyls are colourless, disagreeable-smelling liquids, fuming strongly in the air and igniting readily ; therefore, they can only be handled in an atmosphere of carbon dioxide. They inflict painful wounds when brought into contact with the skin.

Reactions.—The zinc alkyls are exceedingly reactive.

(1) Water decomposes them very energetically, forming hydrocarbons and zinc hydroxide (see Methane, Ethane, pp. 92, 93).

(2) Oxygen is taken up by slow oxidation in the air, and compounds, *e.g.* $(CH_3)_2ZnO_2$, analogous to peroxides, are produced ; they explode readily and liberate iodine from potassium iodide (Ber. **23**, 394).

(3) The alcohols convert the zinc alkyls into zinc alcoholates and hydrocarbons ; according to relative quantities of the reacting bodies, ethyl zinc ethoxide or zinc alcoholate is formed, together with ethane (C. 1901, II. 1200).



$$Zn(C_2H_5)_2 \longrightarrow Zn\begin{matrix}<O{\cdot}C_2H_5\\ <C_2H_5\end{matrix} \longrightarrow Zn\begin{matrix}<O{\cdot}C_2H_5\\ <O{\cdot}C_2H_5\end{matrix}.$$

(4) The free halogens decompose both the zinc alkyls and those of other metals very energetically :

$$Zn(C_2H_5)_2 + 2Br_2 = 2C_2H_5Br + ZnBr_2.$$

(5) They react with chlorides of the heavy metals and the non-metals, whereby alkyl derivatives of the latter are produced (p. 218).

(6) The zinc alkyls absorb sulphur dioxide and are converted into the zinc salts of the sulphinic acids (p. 177).

(7) Nitric oxide and zinc diethyl produce the zinc salt of the so-called dinitroethylic acid, $C_2H_5{\cdot}N_2O_2H$ (p. 206).

The application of the zinc alkyls is particularly important in nucleus-synthetic reactions :

(8) Hydrocarbons are formed when the zinc alkyls are heated with alkyl iodides (see p. 96).

(9) When zinc alkyls (zinc and alkyl iodides) act on aldehydes, acid chlorides, acid anhydrides (C. 1901, II. 188), ketones, formic esters, acetic esters, lactones, and chlorinated ethers, derivatives of secondary, tertiary, and primary alcohols, as well as of ketones, are produced. The alcohols (p. 132) and ketones (p. 257) can easily be obtained from them.

The alkyl oxides and the alkylene oxides are, however, not affected by the zinc alkyls (Ber. **17**, 1968 : C. 1901, II. 188), but, on the other hand, the heating together of ethylene oxide and magnesium alkyl halides is a method of synthesis of the primary alcohols (p. 134).

Zinc methyl, $Zn(CH_3)_2$, b.p. 46° ; $D_{10} = 1{\cdot}386$, and *Zinc ethyl*, $Zn(C_2H_5)_2$, b.p. 118° ; $D_{18} = 1{\cdot}182$, both solidify when cooled (Ann. **261**, 59).

Zinc propyl, $Zn(CH_2CH_2CH_3)_2$, b.p. 146°.

Zinc iso*propyl*, $Zn(C_3H_7)_2$, b.p. 136° (Ber. **26**, R. 380).

Zinc iso*butyl*, $Zn(C_4H_9)_2$, b.p. 166° (Ann. **223**, 168).

Zinc iso*amyl*, $Zn(C_5H_{11})_2$, b.p. 210° (Ann. **130**, 122).

20. ALKYL DERIVATIVES OF CADMIUM

Cadmium methyl, $CdMe_2$, b.p. 104°, which closely resembles zinc methyl is most readily obtained by the action of magnesium methyl bromide on anhydrous cadmium bromide (Ber. **50**, 1817).

21. ALKYL DERIVATIVES OF MERCURY

Mercury resembles magnesium in forming two types of alkyl derivatives, the dialkyl compounds HgR_2 and the alkyl halogen compounds HgRI.

Dialkyl Derivatives.—HgR_2. These are best obtained by the action of magnesium alkyl bromides or chlorides, less satisfactorily iodides, on mercuric bromide or chloride (*Preparation*, J.A.C.S. **44**, 153). The compounds HgRX are produced as intermediates. The other methods of formation, from sodium amalgam and alkyl iodides, or mercuric chloride and zinc alkyls are of less practical importance.

Properties.—These compounds are colourless, heavy liquids, possessing a faint, peculiar odour. Their vapours are extremely poisonous. Water and air occasion no change in them, but when heated they ignite easily.

Mercury methyl, $Hg(CH_3)_2$, b.p. 95°, D = 3·069. *Mercury ethyl*, $Hg(C_2H_5)_2$, b.p. 159°, D = 2·44, and at 200° breaks down into Hg and butane, $C_2H_5{\cdot}C_2H_5$. It yields ethane (p. 93) when treated with concentrated sulphuric acid.

Mercury sec.-*butyl*, $Hg[CH(CH_3)(C_2H_5)]_2$, b.p. 91–93°/15 mm., is prepared by electrolytic reduction of methyl ethyl ketone in sulphuric acid solution at 50° with a mercury cathode (Ber. **39**, 3626).

$$2C_4H_8O + Hg + 6H = Hg(C_4H_9)_2 + 2H_2O.$$

The **mercury alkyl halides** are formed (1) by the action of mercury on alkyl iodides in sunlight, (2) from the dialkyl mercury derivatives—(*a*) by the action of halogens ; (*b*) by the action of the halogen acids ; (*c*) by the action of mercuric chloride.

Mercury methyl iodide, CH_3HgI, m.p. 143°, forms shining needles, and is insoluble in water. Silver nitrate changes it to *methyl mercury nitrate*, $CH_3{\cdot}Hg{\cdot}ONO_2$. *Mercury ethyl iodide*, C_2H_5HgI, is decomposed, by sunlight, into mercuric iodide and C_4H_{10}. *Mercury allyl iodide*, C_3H_5HgI, m.p. 135°, is converted by HI into propylene and mercuric iodide, HgI_2.

Moist silver oxide changes the haloid derivatives to hydroxyl compounds :

$$C_2H_5HgCl + AgOH = C_2H_5{\cdot}Hg{\cdot}OH + AgCl.$$

Ethyl mercuric hydroxide, C_2H_5HgOH, is a thick liquid, soluble in water and in alcohol. It reacts strongly alkaline, and forms salts with acids.

Mercury compounds, derivable from glycol, result from the action of ethylene on mercuric salts (Ber. **34**, 2910).

22. ALKYL DERIVATIVES OF CALCIUM

Calcium ethyl iodide is prepared similarly to the magnesium compound from calcium and iodoethane in ether solution. It forms an "etherate," $C_2H_5CaI{\cdot}O(C_2H_5)_2$, which is a white amorphous powder, soluble with difficulty in ether. It generates ethane when acted on by water (Ber. **38**, 905).

ORGANIC DERIVATIVES OF ELEMENTS OF GROUP I

The alkyl compounds of the alkali metals cannot be obtained pure from zinc alkyls and sodium ; for their preparation the reaction between an alkali metal and a mercury alkyl in the absence of air, CO_2 and moisture is used (Apparatus, see Ber. **46**, 2845).

$$HgR_2 + 2Na \longrightarrow 2NaR + Hg.$$

They are usually amorphous powders, insoluble in indifferent solvents, and spontaneously inflammable in air (Schlenk, Ber. **50**, 262).

Lithium methyl, LiMe, colourless, microcrystalline powder. *Sodium methyl* and *sodium ethyl*, white powders. Homologues, see Ber. **50**, 262 : *Sodium benzyl*, $Na{\cdot}CH_2C_6H_5$, red, ether-soluble crystals.

The sodium alkyls have been regarded as intermediate compounds in the Wurtz reaction (p. 96).

2 AND 3. ALDEHYDES AND KETONES

The close relationship which exists, on the one hand, between primary alcohols, aldehydes and the carboxylic acids, and on the other hand, between the secondary alcohols and the ketones has been already pointed out.

Aldehydes and ketones resemble each other in containing the carbonyl group ·CO·, but in the former this is combined with one alkyl group and a hydrogen atom, in the latter it is combined with two alkyl groups

$$\underset{\text{Aldehyde.}}{R{\cdot}CO{\cdot}H} \qquad\qquad \underset{\text{Ketone.}}{R{\cdot}CO{\cdot}R'.}$$

Aldehydes and ketones can be regarded as the anhydrides of dihydroxy compounds in which both hydroxyl groups are attached to the same carbon atom. When the formation of a compound containing the group $C(OH)_2$ would be expected in a reaction, with certain exceptions where this compound is stable, the corresponding compound containing the CO group is formed by loss of water. In aqueous solution there is an equilibrium between the two forms,

$$C(OH)_2 \rightleftarrows CO + H_2O.$$

The ethers of the two hydrated forms $R{\cdot}CH(OR')_2$ and $R{\cdot}C(OR')_2{\cdot}R''$ are capable of existence.

The following important methods of preparation are common to aldehydes and ketones :

(1) *Oxidation of the alcohols*, whereby aldehydes are formed from the primary, and ketones from the secondary alcohols.

$$\underset{\substack{\text{Primary}\\\text{alcohol.}}}{R{\cdot}CH_2OH} + O \longrightarrow \underset{\text{Aldehyde.}}{R{\cdot}CHO} + H_2O$$

$$\underset{\text{Secondary alcohol.}}{R{\cdot}CH(OH){\cdot}R' + O} \longrightarrow \underset{\text{Ketone.}}{R{\cdot}CO{\cdot}R'} + H_2O.$$

The above equations represent the end-result, but Wieland has attempted to explain the mechanism of the reaction as follows. He regards the reaction as taking place through the activation of two hydrogen atoms in the alcohol, leading to an equilibrium

$$R{\cdot}CH_2OH \rightleftarrows R{\cdot}CHO + H_2.$$

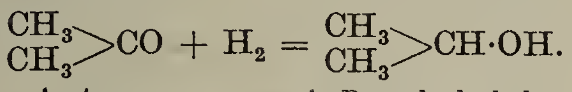
If a " *hydrogen acceptor*," which is capable of uniting with the hydrogen, is present, the equilibrium is shifted from the left to the right of the above equation, and the aldehyde or ketone is formed.

According to Wieland, the oxygen takes a passive part in the reaction, and indeed the reaction can take place in complete absence of free oxygen in the presence of other hydrogen acceptors such as quinone or methylene blue. He was able to convert ethyl alcohol and lactic acid into their oxidation or dehydrogenation products by shaking them in absence of air with finely-divided palladium as a hydrogen activator, and quinone as a hydrogen acceptor (Ber. **45,** 488 : **46,** 3327). Biological oxidations apparently follow a similar mechanism (Ber. **47,** 2806 : for a critical exposition of the Wieland theory, see Z. angew. Chem. **40,** 1130).

By further oxidation the aldehydes become changed into carboxylic acids whilst the ketones are decomposed.

Conversely, aldehydes and ketones are reconverted into primary and secondary alcohols by an addition of hydrogen :

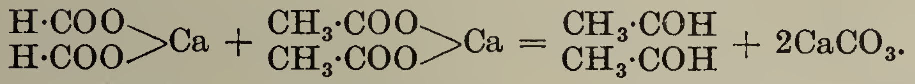
$$\underset{\text{Aldehyde.}}{CH_3\cdot CHO} + H_2 = \underset{\text{Ethyl alcohol.}}{CH_3\cdot CH_2\cdot OH.}$$



$$\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!CO + H_2 = \begin{matrix}CH_3\\CH_3\end{matrix}\!>\!CH\cdot OH.$$

Acetone. *iso*Propyl alcohol.

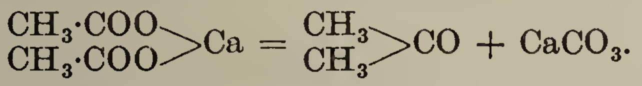
(2) The dry distillation of a mixture of the calcium, or better, barium salts of two monobasic fatty acids produces aldehydes or ketones according as one of the acids be formic acid or not.



$$\begin{matrix}H\cdot COO\\H\cdot COO\end{matrix}\!>\!Ca + \begin{matrix}CH_3\cdot COO\\CH_3\cdot COO\end{matrix}\!>\!Ca = \begin{matrix}CH_3\cdot COH\\CH_3\cdot COH\end{matrix} + 2CaCO_3.$$

Calcium formate. Calcium acetate. Acetaldehyde.

In all other instances ketones result, and they are either simple, with two similar alkyl groups, or mixed, with two dissimilar alkyl groups :



$$\begin{matrix}CH_3\cdot COO\\CH_3\cdot COO\end{matrix}\!>\!Ca = \begin{matrix}CH_3\\CH_3\end{matrix}\!>\!CO + CaCO_3.$$

Acetone.

$$\begin{matrix}CH_3\cdot COO\\CH_3\cdot COO\end{matrix}\!>\!Ca + \begin{matrix}C_2H_5COO\\C_2H_5COO\end{matrix}\!>\!Ca = 2\begin{matrix}C_2H_5\\CH_3\end{matrix}\!>\!CO + 2CaCO_3.$$

Calcium propionate. Ethyl methyl ketone.

On extending this reaction to the calcium salts of adipic, pimelic and suberic acids, *cyclo*paraffin ketones are produced.

(3) Aldehydes and ketones are obtained by direct addition of water to acetylenic hydrocarbons, by the use of suitably diluted sulphuric acid in the presence of mercury salts (see Acetylene, p. 112).

(4) Alkyl hypochlorites, which can be obtained nearly quantitatively from the alcohol, sodium hydroxide and chlorine, decompose under suitable conditions of light and temperature to yield aldehydes and ketones and HCl. The hypochlorites of tertiary alcohols yield ketones and alkyl chlorides (*Chattaway* and *Backeberg*, J.C.S. **123,** 2999).

$$R\cdot CH_2OCl \longrightarrow R\cdot CHO + HCl$$
$$R_2CHOCl \longrightarrow R\cdot CO\cdot R + HCl$$
$$R_3C\cdot OCl \longrightarrow R\cdot CO\cdot R + RCl$$

2A. SATURATED ALDEHYDES. $C_nH_{2n+1}\cdot CHO$

The aldehydes exhibit in their properties a gradation in behaviour similar to that of the alcohols. The lower members are volatile liquids, soluble in water, and have a peculiar odour, but the higher are solids, insoluble in water, and cannot be distilled without decomposition. In general they are more volatile and dissolve with more difficulty in water than the alcohols. Chemically the aldehydes are neutral substances (Ber. **39**, 344).

The reactivity of the aldehydes places them amongst the most important substances for purposes of synthesis, and it is for this reason that the large number of methods for their preparation is being considerably increased, especially during the latter years (Bull. Soc. Chim. [3] **31**, 1306).

Formation and Preparation

(1) *By the oxidation of primary alcohols*, whereby the $—CH_2·OH$ group becomes changed to —CHO (p. 128).

The above oxidation may be effected by atmospheric oxygen in presence of spongy platinum, and by the action of potassium dichromate or MnO_2 and dilute sulphuric acid (Ber. **5**, 699). Chlorine acts similarly in that it first oxidizes the primary alcohols, but then substitutes the alkyl groups of the aldehydes which have been formed (p. 232).

Oxidation of alcohol leads to a good yield of aldehyde with the lower members of the series only, where the product is sufficiently volatile to escape quickly from the region of reaction; otherwise the aldehyde is further oxidized to a carboxylic acid, which in turn unites with some of the unchanged alcohol to form an ester. Even in the case of acetaldehyde, the yield is practically doubled if the reacting mixture is stirred rapidly to disengage the aldehyde as quickly as it is formed.

(2) A direct decomposition of a primary alcohol into H_2 and an aldehyde is brought about by passing alcohol vapours through a red-hot tube, or, better, over finely-divided copper at 200–350° (Ber. **36**, 1990: C. 1905, I. 1002).

The following methods of preparation depend on the reduction of carboxylic acids:

(3) *By heating the calcium salts of fatty acids with calcium formate.* This operation, when working with aldehydes which volatilize with difficulty, should be carried out under diminished pressure (Ber. **13**, 1413).

(4) *By the reduction of acid chlorides and anhydrides by nascent hydrogen,* best from sodium in moist ether (Ber. **29**, R. 662), or catalytically in the presence of nickel or palladium (Ber. **51**, 585: **54**, 2888: **55**, 609).

$$\underset{\text{Acetyl chloride.}}{CH_3·COCl} + 2H = \underset{\text{Acetaldehyde.}}{CH_3·CHO} + HCl.$$

$$\underset{\text{Acetic anhydride.}}{(CH_3·CO)_2O} + 4H = \underset{\text{Acetaldehyde.}}{2CH_3·CHO} + H_2O.$$

Hydrazones of the aldehydes are obtained by reduction of imido-ethers of carboxylic acids by sodium amalgam in acid solution in the presence of hydrazines (Ber. 38, 1362): for formation of aldehydes from anhydrides by means of the diphenylamidines, see Ber. **41**, 2064.

In accordance with methods (3) and (4) the aldehydes may be viewed as hydrides of the acid radicals.

(5) *From the nitriles of the fatty acids,* by way of their imino-chlorides. The nitrile is added to an ethereal solution of stannous chloride saturated with HCl. After a few minutes the crystalline stannichloride of the aldimine separates, and can be hydrolysed by water and the aldehyde extracted with a solvent or distilled off in

steam. With some of the higher nitriles, the yield is practically quantitative (*Stephen*, J.C.S. **127**, 1874).

$$\mathrm{R\cdot CN + HCl \longrightarrow R\cdot CCl : NH}$$

(Iminochloride.)

$$\mathrm{R\cdot CCl : NH + SnCl_2 + 2HCl \longrightarrow R\cdot CH : NH\cdot HCl + SnCl_4}$$

(Aldimine hydrochloride.)

$$\mathrm{R\cdot CH : NH + H_2O \longrightarrow R\cdot CHO + NH_3}$$

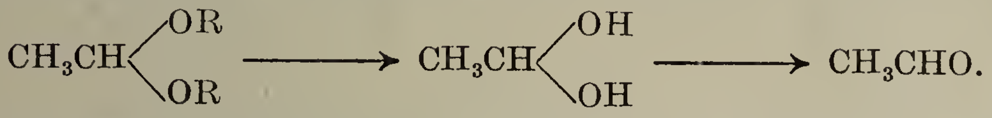
(6) The preparation of aldehydes by *hydrolysis of some of their derivatives* is of great practical importance.

(*a*) from aldehyde-ammonia and aldehyde-bisulphite compounds (see below); from oximes and hydrazones (pp. 250, 252);

(*b*) from aldehyde chlorides (p. 243) by heating them with water and lead oxide:

$$\mathrm{CH_3CHCl_2 \longrightarrow CH_3CH(OH)_2 \longrightarrow CH_3CHO;}$$

(*c*) from ethers and esters of aldehyde hydrates, the acetals and alkylidene diacetates, by means of dilute alkalis or acids:



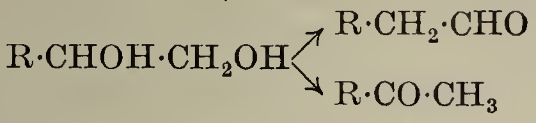
$$\mathrm{CH_3CH{<}^{OR}_{OR} \longrightarrow CH_3CH{<}^{OH}_{OH} \longrightarrow CH_3CHO.}$$

In the course of these reactions αα-glycols, dihydroxyl compounds, should be formed; if they are, they instantly give up water and pass into aldehydes (p. 46).

(7) *From αβ-glycols or their ethers*, containing at least one primary alcohol group, by loss of water or alcohol, or from the corresponding ethylene oxide, by intramolecular isomeric change.

(*a*) Ethylene glycol yields acetaldehyde when heated with dilute sulphuric acid or other dehydrating agents.

(*b*) Primary-secondary glycols yield under the same conditions a mixture of aldehyde and ketone:

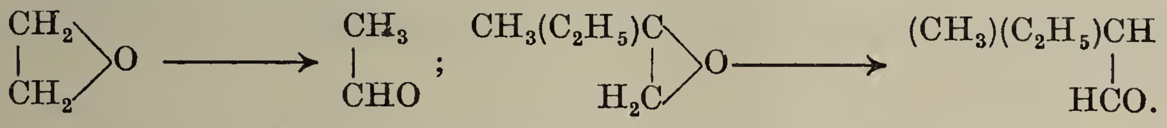


$$\mathrm{R\cdot CHOH\cdot CH_2OH{<}^{\nearrow R\cdot CH_2\cdot CHO}_{\searrow R\cdot CO\cdot CH_3}}$$

(*c*) Primary-tertiary ethylene glycols yield aldehydes when heated with anhydrous formic and oxalic acid; the ethers, $\mathrm{R_2C(OH)\cdot CH_2OR}$, react particularly easily (Ber. **39**, 2288: Ann. Chim. Phys. [8] **9**, 484):

$$\mathrm{R_2C(OH)\cdot CH_2OC_2H_5 = R_2CH\cdot CHO + C_2H_5OH.}$$

(*d*) Ethylene oxide and its homologues, especially the primary-tertiary compounds, undergo internal rearrangement when heated with zinc chloride, or alone (Ber. **36**, 2016), or by passing their vapour over heated $\mathrm{Al_2O_3}$ (Ber. **56**, 2178):



(8) The sodium salts of the primary nitroparaffins yield aldehydes and $\mathrm{N_2O}$ when treated with acids. Nitro-olefines of the formula $\mathrm{RCH{=}CHNO_2}$ on reduction yield oximes of the aldehydes (C. 1903, II. 553):

$$\mathrm{(CH_3)_2C : CHNO_2 \xrightarrow{H} (CH_3)_2CH\cdot CH : NOH \longrightarrow (CH_3)_2CH\cdot CHO.}$$

(9) Aldehydes are obtained by the action of alkalis on the dialkylchloroamines, R_2NCl (see p. 200), and nitramines, $R_2N{\cdot}NO_2$ (see p. 201).

(10) Aldehydes and their derivatives are obtained by means of a *Grignard synthesis*, by the action of magnesium alkyl halides containing one carbon atom less than the required aldehyde on excess of various formic acid derivatives (Ann. **347,** 348 : Ber. **37,** 186, 875 : C. 1904, I. 1077 : 1905, I. 219) :

$$R{\cdot}MgX + \underset{\text{Ester.}}{H{\cdot}COOEt} \longrightarrow \underset{\text{Aldehyde.}}{R{\cdot}CHO} + X{\cdot}MgOEt$$

$$R{\cdot}MgX + \underset{\text{Dialkylamide.}}{H{\cdot}CO{\cdot}NR'_2} \longrightarrow \underset{\text{Aldehyde.}}{R{\cdot}CHO} + X{\cdot}MgNR'_2$$

$$R{\cdot}MgX + \underset{\text{Orthoformic ester.}}{H{\cdot}C(OEt)_3} \longrightarrow \underset{\text{Acetal.}}{R{\cdot}CH(OEt)_2} + X{\cdot}MgOEt$$

$$R{\cdot}MgX + \underset{\text{Imidoether.}}{C_6H_5N : CHOEt} \longrightarrow \underset{\text{Aldimine.}}{R{\cdot}CH : NC_6H_5} + X{\cdot}MgOEt.$$

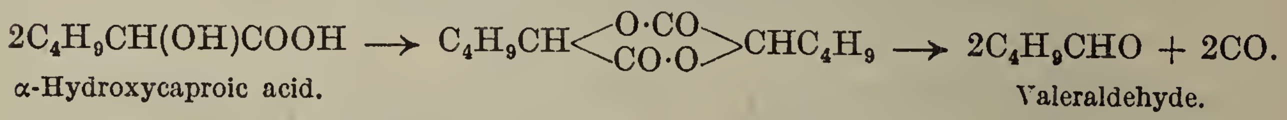
The salts of formic acid also yield some aldehyde when treated with magnesium alkyl halides (C. 1901, II. 765).

(11) *αβ-olefine aldehydes*, or better their acetals, yield paraffin aldehydes on reduction (Ber. **31,** 1900). Since the olefine aldehydes result from condensation of the lower paraffin aldehydes (p. 253) this also constitutes a method of passing synthetically up the aldehyde series.

Conversely, the following degradation reactions may be employed in the production of aldehydes.

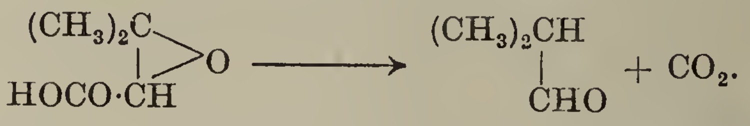
(12) *α-Hydroxycarboxylic acids*, RCH(OH)COOH, which are easily obtained from the fatty acids, yield aldehydes and formic acid (or $CO + H_2O$) by treatment with sulphuric acid. A better method is to heat the hydroxy-acids, converting them by loss of water into lactides, and to distil these, so that they lose CO and pass into aldehydes (C. 1904, I. 1065) :

$$\underset{\text{Lactic acid.}}{CH_3CH(OH)COOH} = \underset{\text{Acetaldehyde}}{CH_3CHO} + \underset{\text{Formic acid.}}{HCOOH.}$$



$$\underset{\alpha\text{-Hydroxycaproic acid.}}{2C_4H_9CH(OH)COOH} \longrightarrow C_4H_9CH{<}\substack{O{\cdot}CO\\CO{\cdot}O}{>}CHC_4H_9 \longrightarrow \underset{\text{Valeraldehyde.}}{2C_4H_9CHO} + 2CO.$$

Connected with this reaction is the formation of aldehydes by heating ethylene oxide carboxylic acids, or glycidic acids, whereby ethylene oxides are formed which become rearranged (Method of formation, 7*d*, p. 227) into aldehydes (C. 1906, II. 1297).



$$\begin{matrix}(CH_3)_2C\\|\\HOCO{\cdot}CH\end{matrix}{>}O \longrightarrow \begin{matrix}(CH_3)_2CH\\|\\CHO\end{matrix} + CO_2.$$

Similarly, α-ketonic acids when heated with dilute sulphuric acid yield aldehyde $+ CO_2$.

$$CH_3COCOOH \longrightarrow CH_3CHO + CO_2.$$

(13) *α-Amino acids* give *N*-chloro acids when treated with sodium hypochlorite, the alkali salts of which break down with formation of an aldehyde when heated in aqueous solution (Ber. **42,** 2360) :

$$R{\cdot}CH(NH_2)COOH \longrightarrow R{\cdot}CH(NHCl)COONa \longrightarrow R{\cdot}CHO$$

(14) Olefines absorb ozone to form ozonides (p. 106), which may be decomposed by water, as follows (Ann. **343**, 311):

$$\underset{\text{Oleic acid.}}{CH_3[CH_2]_7CH : CH[CH_2]_7COOH} \longrightarrow \underset{\text{Nonyl aldehyde.}}{CH_3[CH_2]_7CHO} + \underset{\text{Azelaic aldehydic acid.}}{OCH[CH_2]_7COOH}.$$

This reaction is particularly important for the determination of constitution and for the preparation of dialdehydes and ketone-aldehydes.

Aldehydes occur frequently among the decomposition products of complex carbon compounds, such as proteins, as the result of their oxidation with manganese dioxide or dichromate and dilute sulphuric acid.

Nomenclature and Isomerism.—Empirically, the aldehydes are distinguished from the alcohols by possessing two atoms less of hydrogen—hence their name, suggested by Liebig (from Alcohol dehydrogenatus).

In the " Geneva nomenclature " the names of the aldehydes are formed from the corresponding saturated hydrocarbons by the addition of the suffix *al*; thus acetaldehyde would be termed *ethanal.*

As there is an aldehyde corresponding with every primary alcohol, the number of isomeric aldehydes of definite carbon content equals the number of possible primary alcohols having the same carbon content (p. 128). The aldehydes are isomeric with the ketones, the unsaturated olefine alcohols, and the anhydrides of the ethylene-glycol series, containing an equal number of carbon atoms, *e.g.*:

$$\underset{\text{Propionaldehyde.}}{CH_3{\cdot}CH_2{\cdot}CHO} \text{ isomeric with } \underset{\text{Acetone.}}{CH_3{\cdot}CO{\cdot}CH_3} \quad \underset{\text{Allyl alcohol.}}{CH_2{=}CHCH_2OH}$$

$$\underset{\text{Trimethylene oxide.}}{CH_2{<}\begin{matrix}CH_2\\CH_2\end{matrix}{>}O}$$

Reactions of the Aldehydes

(1) *Oxidation.*—On oxidation aldehydes are readily converted into the carboxylic acid with the same number of carbon atoms, and consequently they behave as powerful reducing agents:

$$R{\cdot}CHO + O \longrightarrow R{\cdot}COOH.$$

Like the formation of aldehydes from alcohols, this reaction is regarded by Wieland as a dehydrogenation of the aldehyde hydrate:

$$R{\cdot}CH(OH)_2 \longrightarrow R{\cdot}COOH + 2H.$$

On the other hand, the auto-oxidation of aldehydes on exposure to air is a direct addition of molecular oxygen to the molecule, with formation of a per-acid, which then reacts with a further molecule of aldehyde to form two molecules of carboxylic acid. The presence of the per-acid in the reacting mixture can be shown by the liberation of iodine from a potassium iodide solution (see Ber. **29**, 1454: **33**, 1581):

$$R{\cdot}CHO + O_2 \longrightarrow R{\cdot}C{<}\begin{matrix}O\\O{\cdot}OH.\end{matrix}$$

The ready oxidizability of the aldehydes forms the basis for some important methods for their detection. If an aldehyde is warmed with a dilute ammoniacal silver solution, silver is precipitated in the form of a silver mirror on the walls of the vessel. Aldehydes reduce Fehling's solution, with the formation of cuprous oxide.

(2) *Colour Reactions. Schiff's Reaction.*—Aldehydes are readily differentiated from ketones by Schiff's reagent. (A solution of rosaniline (magenta) which has just been decolorized by sulphurous acid.) On adding an aldehyde to this reagent, a pink or violet colour is produced. Ketones give no colour with Schiff's reagent (Mechanism of reaction, see Ber. **54**, 2527).

Reaction of Angeli-Rimini.—Aldehydes form hydroxamic acids, $R{\cdot}C(:NOH){\cdot}OH$, which give a red colour with ferric chloride, when treated with the salts of nitrohydroxamic acid, $HO{\cdot}N:NOONa$, and benzenesulphohydroxamic acid, $C_6H_5{\cdot}SO_2{\cdot}NHONa$ (Gazzetta, **34**, I. 56: Atti. R. Accad. Lincei. [5] **17**, II. 360).

(3) *Condensations.*—Dilute alkaline solutions, including potassium cyanide, sodium acetate, etc., cause aldehydes containing the groups $\cdot CH_2{\cdot}CHO$ and $>CH{\cdot}CHO$ to undergo the "*aldol condensation*" to hydroxy-aldehydes (see p. 390). Concentrated alkalis resinify the lower aldehydes, especially acetaldehyde. (See also (10), p. 232.)

Where the aldol condensation is impossible, some aldehydes, particularly the aromatic aldehydes, undergo a "Cannizzaro reaction" yielding equimolecular amounts of the corresponding alcohol and acid. Among the aliphatic aldehydes, *iso*butyraldehyde undergoes this reaction under the influence of baryta water (C. 1901, II. 762). This may be due to the intermediate formation of a molecule of ester, which is then hydrolysed by the baryta:

$$2R{\cdot}CHO \longrightarrow R{\cdot}CH_2O{\cdot}CO{\cdot}R \xrightarrow{H_2O} R{\cdot}CH_2OH + R{\cdot}COOH.$$

Evidence for the intermediate formation of esters is given by the fact that anhydrous condensing agents such as the aluminium alkoxides produce esters from the lower aldehydes. Thus, trioxymethylene gives with aluminium methoxide, methyl formate, and acetaldehyde, ethyl acetate. (This is of technical importance in the preparation of acetic ester from acetylene.) (C. 1906, II. 1552.)

The so-called "*acyloin*" condensation, whereby α-keto alcohols are produced from two molecules of aldehyde, is of great importance with aromatic aldehydes, but does not occur chemically in the aliphatic series. In fermentation reactions, the nascent aldehyde formed is regarded as undergoing an acyloin condensation with other aldehydes. The enzyme which carries out this synthesis is called carboligase (Ber. **57**, 1436):

$$\underset{\text{(Nascent.)}}{CH_3{\cdot}CHO} + CH_3{\cdot}CHO \longrightarrow CH_3{\cdot}CHOH{\cdot}CO{\cdot}CH_3.$$

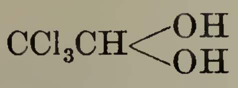
(4) *Polymerization.*—The lower members of the homologous series of the aldehydes polymerize very readily. The polymerization of the aldehydes and thioaldehydes depends on the union of several aldehyde radicals, $CH_3{\cdot}CH=$, through the oxygen or sulphur atoms (Ann. **203**, 44). This phenomenon will be fully treated under formaldehyde and acetaldehyde (pp. 236, 237).

(5) *Addition Reactions.*—(*a*) *Addition of Hydrogen.* By the action of nascent hydrogen, or catalytically in the presence of a nickel catalyst at 140°, aldehydes are reduced to primary alcohols (Compt. rend. **137**, 301):

$$R{\cdot}CHO + 2H \longrightarrow R{\cdot}CH_2OH.$$

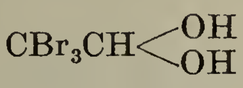
A small quantity of α-glycol is produced as a by-product, by the combination of two molecules (Atti. R. Accad. Lincei. [5] 22, II. 681).

(*b*) *Addition of Water.*—Ordinarily, aldehydes do not combine with water (comp. p. 241). The polyhalogen aldehydes, *e.g.* chloral, bromal, butyl chloral (pp. 238, 240), however, have this power, and yield feeble and readily decomposable *hydrates*, representatives of dihydroxy alcohols, both hydroxyl groups of which are attached to the same carbon atom :



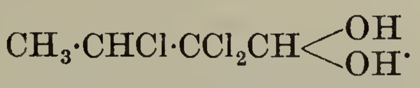
$$\mathrm{CCl_3CH}<\begin{matrix}\mathrm{OH}\\\mathrm{OH}\end{matrix}$$

Chloral hydrate.



$$\mathrm{CBr_3CH}<\begin{matrix}\mathrm{OH}\\\mathrm{OH}\end{matrix}$$

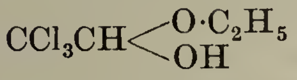
Bromal hydrate.



$$\mathrm{CH_3{\cdot}CHCl{\cdot}CCl_2CH}<\begin{matrix}\mathrm{OH}\\\mathrm{OH}\end{matrix}.$$

Butyl chloral hydrate.

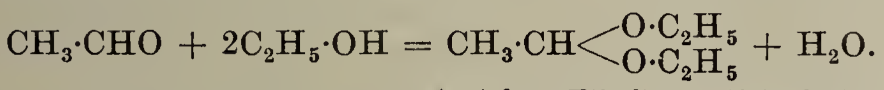
(*c*) *Addition of Alcohols.*—It is also only the polyhalogen aldehydes, *e.g.* chloral, which unite with alcohols, forming aldehyde-alcoholates :



$$\mathrm{CCl_3CH}<\begin{matrix}\mathrm{O{\cdot}C_2H_5}\\\mathrm{OH}\end{matrix}$$

Chloral alcoholate.

The ordinary aldehydes yield acetals with the alcohols at 100° (p. 241) :



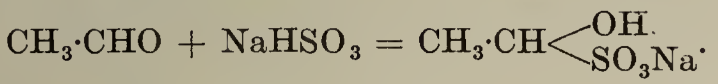
$$\mathrm{CH_3{\cdot}CHO + 2C_2H_5{\cdot}OH = CH_3{\cdot}CH}<\begin{matrix}\mathrm{O{\cdot}C_2H_5}\\\mathrm{O{\cdot}C_2H_5}\end{matrix} + \mathrm{H_2O}.$$

Acetal or Ethylidene diethyl ether.

(*d*) *Addition of Acid Anhydrides.*—Aldehydes combine with acid anhydrides to form the esters of the hydrated form of the aldehyde, the αα-glycol :

$$\mathrm{R{\cdot}CHO + (R'CO)_2O \longrightarrow R{\cdot}CH(O{\cdot}COR')_2}.$$

(*e*) Aldehydes unite in a similar manner with *alkali bisulphites*, forming crystalline compounds :



$$\mathrm{CH_3{\cdot}CHO + NaHSO_3 = CH_3{\cdot}CH}<\begin{matrix}\mathrm{OH}\\\mathrm{SO_3Na}\end{matrix}.$$

(*Constitution*, see p. 244). The aldehydes may be liberated from these salts by distillation with dilute sulphuric acid or aqueous sodium hydroxide. This procedure permits of the separation and purification of aldehydes from other substances.

(*f*) *Reaction with Hydrogen Sulphide and Mercaptans.*—In the presence of hydrochloric acid, hydrogen sulphide converts aldehydes into the trithioaldehyde. Mercaptans, under the action of hydrochloric acid, produce mercaptals, $\mathrm{R{\cdot}CH(S{\cdot}R)_2}$ (see p. 247).

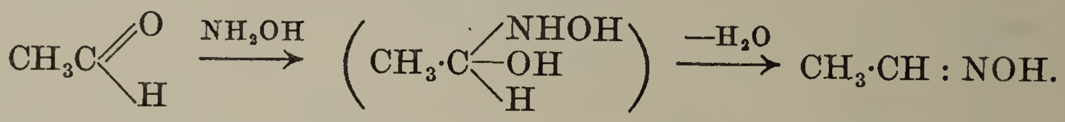
(*g*) *Addition of hydrocyanic acid* and *Grignard reagents*, see p. 233.

(6) *Typical Reactions of the* $>$CO (*Carbonyl*) *Group.*—Behaviour of aldehydes with *ammonia*, *primary alkylamines*, *hydroxylamine*, and *phenylhydrazine* ($\mathrm{C_6H_5{\cdot}NH{\cdot}NH_2}$). (*a*) They unite directly with *ammonia* to form crystalline compounds, called aldehyde-ammonias $\mathrm{R{\cdot}CH(OH){\cdot}NH_2}$. These are readily soluble in water but not in ether, hence ammonia gas will precipitate them in crystalline form from the ethereal solution of the aldehydes. They are rather unstable, and dilute acids again resolve them into their components. Pyridine bases are produced when the aldehyde-ammonias are heated.

(*b*) Aldehydes and *primary amines* combine, with loss of water, to form aldimines, $\mathrm{R{\cdot}CH:NH}$ (p. 248).

(*c*) The aldehydes react with *hydroxylamine* to form *aldoximes* with accompanying liberation of water (*V. Meyer*, Ber. 15, 2778).

It is evident that at first, in these cases, there is formed an unstable intermediate product (compare chloral hydroxylamine, p. 251) corresponding with aldehyde-ammonia :



$$\mathrm{CH_3C}\begin{smallmatrix}\nearrow \mathrm{O}\\ \searrow \mathrm{H}\end{smallmatrix} \xrightarrow{\mathrm{NH_2OH}} \left(\mathrm{CH_3\cdot C}\begin{smallmatrix}\nearrow \mathrm{NHOH}\\ -\mathrm{OH}\\ \searrow \mathrm{H}\end{smallmatrix}\right) \xrightarrow{-\mathrm{H_2O}} \mathrm{CH_3\cdot CH : NOH}.$$

(*d*) The aldehydes behave similarly with *phenylhydrazine* ; water separates and *phenylhydrazones* (*E. Fischer*) result (p. 253) :

$$\mathrm{CH_3\cdot CHO + H_2N\cdot NHC_6H_5 = CH_3\cdot CH : N\cdot NHC_6H_5 + H_2O}.$$

These substances serve well for the detection and characterization of the aldehydes. The aldoximes and hydrazones, when boiled with acids, absorb water and revert to their parent substances. They yield primary amines when reduced (p. 190).

(*e*) *Hydrazine, semicarbazide* (*q.v.*), *p-amino-dimethylaniline* (Ber. **17**, 2939), *aminophenols*, and other aromatic bases (*Schiff*, Ber. **25**, 2020) react with aldehydes, similarly to phenylhydrazine and its substitution products.

(7) Compounds are formed by the action of phosphorus trichloride on aldehydes, which are converted by water into hydroxalkyl phospho-acids, *e.g.* $CH_3\cdot CH(OH)PO(OH)_2$ (Ber. **18**, R. 111).

(8) *Phosphorus pentachloride* and phosphorus trichloro-dibromide cause the replacement of the aldehyde oxygen by chlorine or bromine and yield dichlorides and dibromides, in which the two halogen atoms are linked to a terminal carbon atom (p. 243) :

$$\mathrm{CH_3CHO + PCl_5 = CH_3CHCl_2 + POCl_2}.$$

(9) The hydrogen atoms of the alkyl groups of the aldehydes may be replaced by the action of bromine, as well as by iodine and iodic acid.

B. Nuclear Synthetic Reactions of the Aldehydes

(10) *Aldol Condensation.*—Aldehydes which contain at least one hydrogen atom linked to the carbon atom adjacent to the ·CHO group are able under suitable conditions, such as the action of zinc chloride or dilute alkalis, to undergo an "*aldol condensation*" whereby two or more aldehyde molecules become linked by a new *carbon* linkage. The "aldols" so formed are aldehyde-alcohols, *e.g.* from acetaldehyde, aldol or *β*-hydroxybutyraldehyde is formed (*Wurtz*) :

$$\mathrm{CH_3\cdot CHO + CH_3\cdot CHO \longrightarrow CH_3\cdot CH(OH)\cdot CH_2\cdot CHO}.$$

A similar aldol condensation is also possible between two different aldehydes :

$$\mathrm{R\cdot CH_2\cdot CHO + R'\cdot CH_2\cdot CHO \longrightarrow R\cdot CH_2\cdot CH(OH)\cdot CHR'\cdot CHO}.$$

A similar type of condensation can also take place between aldehydes and other compounds such as ketones, malonic ester, cyanoacetic ester, etc., which contain an active $\cdot CH_3$, $: CH_2$ or $\vdots\, CH$ group adjacent to a CO group :

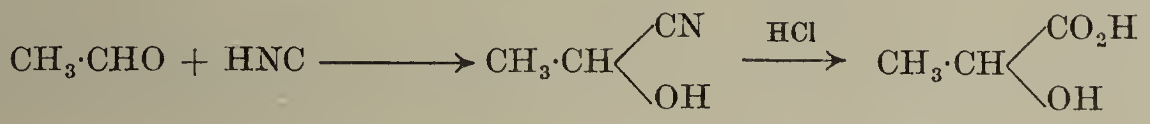
$$\mathrm{R\cdot CHO + CH_2(CO_2Et)_2 \longrightarrow R\cdot CH(OH)\cdot CH(CO_2Et)_2}.$$

In many cases, the first-formed hydroxy compound loses water, and an unsaturated compound is the isolated product :

$$\mathrm{R\cdot CH(OH)\cdot CH(CO_2Et)_2 \longrightarrow R\cdot CH : C(CO_2Et)_2}.$$

(11) *Grignard Syntheses.*—Aldehydes react with zinc alkyls or with magnesium alkyl halides to form addition products, which when decomposed by water or acids yield secondary alcohols (see p. 132).

(12*a*) Aldehydes also combine with hydrogen cyanide, yielding hydroxy-cyanides or *cyanhydrins*. These are the nitriles of α-hydroxy-acids (*q.v.*), which will be discussed after the α-hydroxy-acids themselves, and which can be converted into the acids by means of hydrochloric acid :

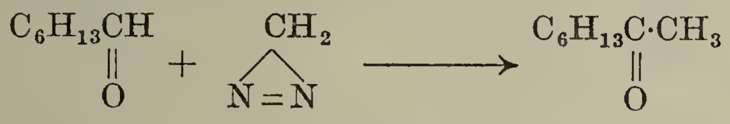


$$CH_3{\cdot}CHO + HNC \longrightarrow CH_3{\cdot}CH{<}^{CN}_{OH} \xrightarrow{HCl} CH_3{\cdot}CH{<}^{CO_2H}_{OH}$$

Lactic acid.

(*b*) Aldehydes and ammonium cyanide react together, when water separates, and the *nitriles* of *α-amino-acids*, *e.g.* $CH_3{\cdot}CH{<}^{NH_2}_{CN}$, result. When treated with hydrochloric acid they yield amino-acids (*q.v.*). The same amino-nitriles are produced by the action of CNH on the aldehyde-ammonias, and from the hydroxy-cyanides and ammonia. Nitriles of α-anilino-, α-phenylhydrazino-, and α-oximino-acids are formed by the addition of hydrocyanic acid to the aliphatic aldehyde-anilines, aldehyde phenylhydrazones and aldoximes (Ber. **25**, 2020).

(13) Diazomethane (p. 251) and aldehydes produce alkyl-methyl ketones, with evolution of nitrogen, and probably with the formation of an intermediary addition product (Ber. **40**, 479, 847) :



With certain " negatively substituted " aldehydes such as chloral, instead of ketones, ethylene oxides are formed by the action of diazomethane (Z. angew. Chem. **40**, 1099).

Aromatic diazo-compounds react similarly with many aldoximes, forming fatty-aromatic ketoximes (Ber. **40**, 737).

Formaldehyde, *Methyl aldehyde* [methanal], H·CHO, m.p. about $-92°$ (Ber. **34**, 635), b.p. about $-21°$, $D_{-80} = 0{\cdot}9172$, $D_{-20} = 0{\cdot}8153$, was discovered by *A. W. Hofmann*, and was until recently only known in aqueous solution and in vapour form. It may, as was shown by *Kekulé*, be condensed, by lowering the temperature to a colourless liquid. Liquid formaldehyde changes slowly at $-20°$, rapidly at the ordinary temperature, the reaction being facilitated by the presence of traces of water, into trioxymethylene, $(CH_2O)_3$ (Ber. **25**, 2435). This polymeric modification was known before the simple formaldehyde, into which it is changed by heat. Formaldehyde possesses a sharp, penetrating odour, and destroys bacteria of the most varied types ; it is, therefore, applied (under the name of *formalin*) either in solution or as a gas, for disinfecting purposes. Many of its compounds with organic bodies are suitable for this purpose, as they regenerate formaldehyde more or less easily (Ber. **27**, R. 757, 803 : **28**, R. 938 : **29**, R. 178, 288, 426 : C. 1900, I. 263, 791, etc.).

Another technically important use of formaldehyde is based on its power to form compounds with proteins. One of these, with casein, so-called " galalith," is used as a substitute for ivory, horn, etc. The use of formaldehyde in the tanning industry and for the manufacture of photographic plates depends upon this reaction. An artificial composition of the name "Bakelite" is produced on the large scale by the condensation of formaldehyde with phenol at high temperatures. A derivative of formaldehyde, sodium formaldehydesulphoxylate, which is obtained from formaldehyde, sodium bisulphite and zinc dust is much used in the dye industry under the names Rongalite, Hydralite, etc. (see p. 245).

Methods of Formation.—(1) It is produced when the vapours of methyl alcohol, mixed with air, are conducted over an ignited platinum spiral or ignited copper gauze (J. pr. Chem. **33,** 321 : Ber. **19,** 2133 : **20,** 144 : Ann. **243,** 335) : lamps have been constructed for this purpose (Ber. **28,** 261).

This reaction depends on a catalytic decomposition of the alcohol into formaldehyde and hydrogen, the latter then being burned by the admixed oxygen (Z. Elektrochem. **17,** 45).

Technically, formaldehyde is manufactured from methyl alcohol by this method, fine silver gauze acting as the catalyst.

(2) Formaldehyde can be obtained in about 50% yield by passing a mixture of acetaldehyde and air over suitable metallic catalysts, such as copper wire (Brit. Pat. 178842, J.C.S. Abstr. 1923, i, 752).

(3) Formaldehyde can also be obtained by passing a mixture of methane and CO_2 through constricted metallic tubes at 500–700° in about 56% yield. The following reactions occur (Brit. Pat. 156148, J.C.S. Abstr. 1922, i, 522) :

$$2CO_2 \longrightarrow 2CO + 2O$$
$$CH_4 + 2O \longrightarrow H{\cdot}CHO + H_2O.$$

(4) Formaldehyde is produced by the action of halogens on methyl alcohol (Ber. **26,** 268) : further action of these decomposes the formaldehyde into CO and halogen acid.

(5) It is produced in small quantity by heating calcium formate or zinc formate (Ber. **51,** 1398).

(6) In addition to its production from CO_2 and CO and hydrogen under the action of metallic catalysts, formaldehyde is obtained in small quantity by the action of ultra-violet light or the silent electric discharge on the mixed gases (see Z. Elektrochem. **12,** 412 : Chem. Ztg. **34,** 945 : Proc. Roy. Soc. **84** [B] 101 : J.C.S. **119,** 1025). This observation is of great interest, as, since 1870, when Baeyer first made the suggestion (Ber. **3,** 63) that formaldehyde was the first product of photosynthesis in the plant, this reaction has been generally accepted as the first step in the production of carbohydrates from carbon dioxide in the plant.* Some indirect support has been given to this by the observations of Willstätter on the assimilation quotient, *i.e.* the ratio of O_2 produced to CO_2 absorbed, was 1, which is in agreement with the equation $H_2CO_3 \longrightarrow H{\cdot}CHO + O_2$. Recently, the formation of a compound from formaldehyde and dimethyldi-

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* Critical summary of work on this subject, see *R. Willstätter* and *A. Stoll* : Untersuchungen über die Assimilation der Kohlensäure (Berlin, 1918) : *H. Schröder* : Die Hypothese über die Vorgänge bei der Kohlensäure Assimilation (Jena, 1917).

hydroresorcinol has been made the basis of an attempt to show directly the formation of formaldehyde in photosynthesis (Klein, Biochem. Z. **168**, 361), but doubt has been cast on the interpretation of these results (Biochem. J. **24**, 1210). For the present, the formation of formaldehyde in photosynthesis must be regarded as probable, but unproven.

(7) Formaldehyde is produced by the partial oxidation of various hydrocarbons by passing them through heated tubes with oxygen suitably diluted. Thus, under suitable conditions, a 75% yield of formaldehyde can be obtained from ethylene and oxygen (Blair and Wheeler, J. Soc. Chem. Ind. 1922, **41**, 303T).

Detection and Estimation of Formaldehyde.—The majority of methods for the detection of formaldehyde depend upon its capacity to form sparingly soluble condensation products with aromatic amines and polyhydric phenols, particularly with resorcinol and phloroglucinol (Ann. **299**, 317 : C. 1889, I. 270). A strong acid solution of fuchsin-sulphurous acid gives a blue or blue-violet colour with formaldehyde (Ann. **404**, 105). For the separation of small quantities of formaldehyde, its condensation product with dimethylhydroresorcinol (Dimedon) is used (Ann. **294**, 314 : Biochem. Z. **106**, 281).

The strength of a solution can be estimated gravimetrically by converting the formaldehyde into hexamethylenetetramine $(CH_2)_6N_4$ (Ber. **16**, 1333 : **22**, 1565, 1929 : **26**, R. 415), or into dimethylene *p*-dihydrazinophenyl (Ber. **32**, 1961).

Titrimetric Methods.—The formaldehyde is transformed by hydrogen peroxide in alkaline solution of known strength into sodium formate and hydrogen, under the influence of its own heat generation :

$$2CH_2O + 2NaOH + H_2O_2 = 2HCO_2Na + 2H_2O + H_2.$$

From the back titration of the unused alkali the quantity of formic acid can be found. The reaction takes place with the intermediate formation of an addition product between 2 mols. of formaldehyde and 1 mol. of hydrogen peroxide (dihydroxymethyl peroxide, $HOCH_2{\cdot}O{\cdot}O{\cdot}CH_2OH$) (see p. 241), which is quantitatively decomposed by sodium hydroxide into sodium formate and water (Ann. **431**, 301) :

$$HOCH_2{\cdot}O{\cdot}O{\cdot}CH_2OH + 2NaOH \longrightarrow 2H{\cdot}COONa + H_2 + H_2O.$$

The estimation can also be carried out by treatment with an alkaline iodine solution and back titration with thiosulphate (C. 1905, I. 630).

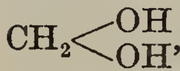
Formaldehyde and sodium sulphite solution unite with liberation of sodium hydroxide, the titration of which gives the quantity of formaldehyde. This reaction can also be employed for the estimation of aldehyde polymers (C. 1904, II. 263).

Reactions.—Dilute solutions of the alkali hydroxides partially transform formaldehyde into formic acid and methyl alcohol (comp. p. 230 and Ber. **38**, 2556). A modified aldol condensation occurs with excess of such alkalis as lime, calcium carbonate, or lead oxide (p. 232), giving rise to glycol aldehyde, $C_2H_4O_2$, *i*-arabinose, $C_5H_{10}O_5$, and various hexoses, $C_6H_{12}O_6$, of which the principal is α-acrose or *dl*-fructose (Ber. **39**, 45, 1592).

It is noteworthy that the condensation of formaldehyde to glycollic aldehyde also takes place under the influence of ultra-violet light (Monatsh. **33**, 415 : J. pr. Chem. [2] **86**, 336). This reaction gives support to the theories of assimilation of carbon dioxide in plants (Ber. **3**, 67 : J. pr. Chem. [2] **33**, 344).

Formaldehyde acted on by acetaldehyde and lime yields pentaerythritol, $C(CH_2OH)_4$ (Ber. **26**, R. 713) ; with nitromethane (p. 181) it gives nitro-*tert.*-butyl glycerol, $NO_2C\cdot(CH_2OH)_3$; with picoline (Vol. III) it yields trimethylolpicoline, $(C_5H_4N)C(CH_2OH)_3$. Thus, formaldehyde shows a strong tendency to unite repeatedly with reactive CH_3-groups, to form aldol-like bodies of increasing complexity.

In the very numerous reactions of formaldehyde its oxygen unites with two hydrogen atoms of the reacting body to yield water. It is immaterial whether the hydrogen is in union with carbon, nitrogen, or oxygen. The products are, for example, diphenylmethane derivatives, methyleneaniline, and formals of polyhydric alcohols (Ann. **289**, 20).

Polymeric Modifications of Formaldehyde.—The concentrated aqueous solution of formic acid not only contains volatile CH_2O, but also the hydrate  $CH_2{<}^{OH}_{OH}$, *i.e.* hypothetical methylene glycol, and non-volatile *polyhydrates*. On complete evaporation of the solution the hydrates condense to the solid water-soluble *paraformaldehyde*, $(CH_2O)_n$.

Trioxymethylene, $(CH_2O)_3$, *metaformaldehyde* (*Butlerow*), is distinguished from the so-called paraformaldehyde, by its insolubility in water, alcohol, and ether. It is formed from the monomeric formaldehyde by evaporation of its solutions over sulphuric acid. On heating, it changes into the monomeric vapour, as shown by determinations of the vapour density. It forms an indefinitely crystalline mass, m.p. 171–172°. When it is heated with water to 130° it changes to the simple molecule CH_2O, but by prolonged heating carbon dioxide and methyl alcohol are produced (Ber. **29**, R. 688).

When dry trioxymethylene is heated with a trace of sulphuric acid to 115° in a sealed tube it is changed into the isomeric α-trioxymethylene, $(CH_2O)_3$, m.p. 60–61° (Ber. **17**, R. 567).

The polymeric modifications of formaldehyde have not yet been as successfully studied as the polymeric acetaldehydes (C. 1904, II. 21, 585).

In contact with peroxides, such as BaO_2 and SrO_2, and in the presence of water, the polymerized formaldehydes are catalytically changed into the simple form accompanied by the disengagement of a considerable quantity of heat (C. 1906, II. 1135).

Acetaldehyde, *Ethyl aldehyde* [ethanal], $C_2H_4O{=}CH_3\cdot CHO$, m.p. − 120°, b.p. 20·8°, $D_0 = 0{\cdot}8009$ (Ber. **23**, 638), is prepared according to the usual methods: (1) From ethyl alcohol; (2) from calcium acetate; (3) from acetyl chloride or acetic anhydride; (4) from ethylidene chloride, from acetal and ethylidene diacetate; (5) from ethylene oxide; (6) from lactic acid; (7) from sodium nitroethane; and (8) from acetylene (p. 110). It occurs in the first runnings in the rectification of spirit, and is formed, too, by the oxidation of alcohol when filtered through wood charcoal (p. 143).

History.—In 1774 *Scheele* noticed that aldehyde was formed when alcohol was oxidized with manganese dioxide and sulphuric acid. *Döbereiner*, however, was the first to isolate the aldehyde in the form of aldehyde-ammonia, which he gave for investigation to *Liebig*, who then established the composition of aldehyde and showed its relation to alcohol. It was Liebig who introduced the name *Al*(cohol)-*dehyd*(*e*)(rogenatus) into chemical science (Ann. **14**, 133: **22**, 273: **25**, 17). Ordinary aldehyde readily polymerizes to liquid *paraldehyde*, and solid *metaldehyde*. *Fehling* first observed the former, and *Liebig* the latter. *Kekulé* and *Zincke* determined the conditions of formation for the aldehyde modifications and cleared up the somewhat confused reaction relations (Ann. **162**, 125).

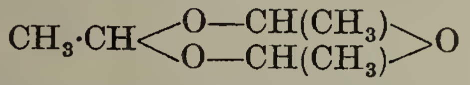
Preparation.—90 per cent. ethyl alcohol (3 parts) is oxidized by dropping into it a mixture of a solution of 3 parts of potassium dichromate in 12 parts of water and 4 parts of concentrated sulphuric acid (Ber. **27**, R. 471). The escaping aldehyde vapours are conducted into ether and aldehyde-ammonia separates in a crystalline form when ammonia is passed into the ethereal solution. Pure aldehyde may be liberated from this by dilute sulphuric acid, and dried over dehydrated calcium chloride.

Acetaldehyde is a mobile, peculiar-smelling liquid, miscible in all proportions with water, ether and alcohol. It is prepared technically in order to obtain paraldehyde and quinaldine (*q.v.*).

Polymeric Aldehydes.—Small quantities of acids (HCl, SO_2) or salts ($ZnCl_2$, CH_3CO_2Na) convert aldehyde at *ordinary temperatures* into **paraldehyde**, $(C_2H_4O)_3$, m.p. 124°, $D_{20} = 0{\cdot}9943$; the change is accompanied by evolution of heat and contraction in volume and is particularly rapid, if a few drops of sulphuric acid be added to the aldehyde. Paraldehyde is a colourless liquid, and dissolves in about 12 vols. H_2O; it is, however, more soluble in the cold than when warm. This behaviour would point to the formation of a hydrate. The vapour density agrees with the formula $C_6H_{12}O_3$. Paraldehyde is employed in medicine as a soporific. When distilled with sulphuric acid ordinary aldehyde is generated. Paraldehyde can be brominated at $-10°$ to $-15°$ to mono- and dibromo-paraldehydes, accompanied by small amounts of tribromo-compound by the use of the appropriate amount of bromine (Ber. **58**, 1718: **59**, 2533).

Metacetaldehyde (*Metaldehyde*), $(C_2H_4O)_4$ or $(C_2H_4O)_{2n}$ (Ber. **40**, 4341), is formed by the action of similar reagents on acetaldehyde at temperatures below 0°. It is a white crystalline compound, insoluble in water, but readily dissolving in hot alcohol and ether. It sublimes without melting at about 150°, with partial decomposition into the monomolecular aldehyde: the decomposition to the monomolecular form is complete when the compound is heated in a sealed tube. If kept at 60–65° for several days, metacetaldehyde changes into acetaldehyde and paracetaldehyde.

Chemical behaviour, refractive power, and specific volume point to a single linkage of oxygen and carbon; therefore the three oxygen atoms in paraldehyde unite the three ethylidene groups to a ring of six members:

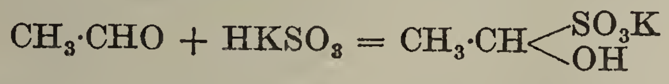


$$CH_3\cdot CH\left<\begin{matrix}O-CH(CH_3)\\ O-CH(CH_3)\end{matrix}\right>O$$

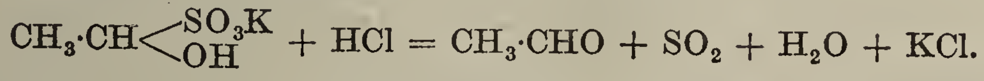
(Ber. **24**, 650; **25**, 3316: **26**, R. 185).

They may be considered cyclic ethers of ethylidene glycol, of which the anhydride is acetaldehyde.

Reactions of Acetaldehyde and its Polymers.—(1) In the air acetaldehyde slowly oxidizes to acetic acid. It produces a silver mirror from an ammoniacal silver nitrate solution. Paraldehyde and metaldehyde do not reduce silver solutions. (2) Alkalis convert acetaldehyde into aldehyde resin. (3) It is reduced to ethyl alcohol by nascent hydrogen. (4) Aldehyde unites with alcohol to form acetal (p. 242). (5) Hydrogen sulphide converts it into thioaldehyde (p. 245), and with mercaptans it forms mercaptals (p. 247). (6) Acetic anhydride changes it to ethylidene diacetate (p. 244). (7) On shaking aldehyde with a very concentrated solution of an alkali bisulphite crystalline compounds separate, $CH_3\cdot CH(OH)SO_3K$, which are resolved into their components when treated with acids (p. 244):



$$CH_3\cdot CHO + HKSO_3 = CH_3\cdot CH\left<\begin{matrix}SO_3K\\ OH\end{matrix}\right.$$



$$CH_3\cdot CH\left<\begin{matrix}SO_3K\\ OH\end{matrix}\right. + HCl = CH_3\cdot CHO + SO_2 + H_2O + KCl.$$

Paraldehyde and metaldehyde do not unite with the bisulphites of the alkalis. (8) Acetaldehyde reacts with ammonia, hydroxylamine, and phenylhydrazine, whilst paraldehyde and metaldehyde fail to do so. (9) Phosphorus pentachloride converts acetaldehyde, paraldehyde and metaldehyde into ethylidene chloride (p. 243).

(10) Aldehyde combines with hydrocyanic acid, the product being the nitrile of *dl*-lactic acid.

For the condensation of aldehyde to aldol, crotonaldehyde, and other compounds, see p. 390.

Homologous Aldehydes

The homologues of formic and acetaldehydes are prepared either (1) by the oxidation of the corresponding primary alcohols ; or (2) by the distillation of the calcium or barium salts of the corresponding fatty acids, mixed with calcium or barium formate ; (3) by transformation of ethylene oxide or glycol ethers ; (4) by organo-magnesium synthesis ; and (5) from the next higher α-hydroxy-fatty acid (C. 1904, II. 509).

Name.	Formula.	M.P.	B.P.
Propionaldehyde [Propanal] . . .	$CH_3CH_2{\cdot}CHO$	—	49°
n-Butyraldehyde [Butanal] . . .	$(CH_3)(CH_2)_2{\cdot}CHO$	—	75°
*iso*Butyraldehyde	$(CH_3)_2CH{\cdot}CHO$	—	61°
n-Valeraldehyde	$(CH_3)[CH_2]_3CHO$	—	103°
*iso*Valeraldehyde	C_4H_9CHO	—	92°
Methylethylacetaldehyde	C_4H_9CHO	—	91°
Trimethylacetaldehyde (Ber. **24**, R. 898)	$(CH_3)_3C{\cdot}CHO$	—	74°
n-Caproic Aldehyde	$CH_3{\cdot}[CH_2]_4CHO$	—	128°
Methyl-*n*-propylacetaldehyde . .	$C_5H_{11}CHO$	—	116°
*iso*Hexaldehyde	$C_5H_{11}CHO$	—	121°
Heptaldehyde, *Œnanthal*	$CH_3[CH_2]_5CHO$	—	155°
Octaldehyde, $C_8H_{16}O$ . . .	$CH_3[CH_2]_6{\cdot}CHO$	—	81° (32 mm.)
Capric Aldehyde, $C_{10}H_{20}O$ . .	$CH_3[CH_2]_8CHO$	—	106° (15 mm.)
Undecaldehyde, $C_{11}H_{22}O$ . .	$CH_3[CH_2]_9{\cdot}CHO$	− 4°	117° (18 mm.)
Lauric Aldehyde, $C_{12}H_{24}O$ . .	$CH_3[CH_2]_{10}CHO$	44·5°	142° (22 mm.)
Tridecaldehyde, $C_{13}H_{26}O$ . .	$CH_3[CH_2]_{11}{\cdot}CHO$	—	152° (24 mm.)
Myristic Aldehyde, $C_{14}H_{28}O$ . .	$CH_3[CH_2]_{12}CHO$	52·5°	168° (22 mm.)
Pentadecaldehyde, $C_{15}H_{30}O$ . .	$CH_3[CH_2]_{13}{\cdot}CHO$	—	185° (25 mm.)
Palmitic Aldehyde, $C_{16}H_{32}O$ . .	$CH_3[CH_2]_{14}CHO$	58·5°	192° (22 mm.)
Margaric Aldehyde, $C_{17}H_{34}O$ . .	$CH_3[CH_2]_{15}CHO$	36°	204° (26 mm.)
Stearic Aldehyde, $C_{18}H_{36}O$ . .	$CH_3[CH_2]_{16}CHO$	63·5°	212° (22 mm.)

Propionaldehyde, by the action of hydrochloric acid, yields both *parapropionaldehyde*, b.p. 169°, and *metapropionaldehyde*, m.p. 180°. They have the molecular formula $(C_3H_6O)_3$ (Ber. **28**, R. 469).

The higher aldehydes also form polymeric forms (Monatsh. **33**, 349).

Of the higher aldehydes, **heptaldehyde** (*œnanthal*, from οἶνος = wine) is most readily obtained, being formed when castor oil is distilled under reduced pressure :

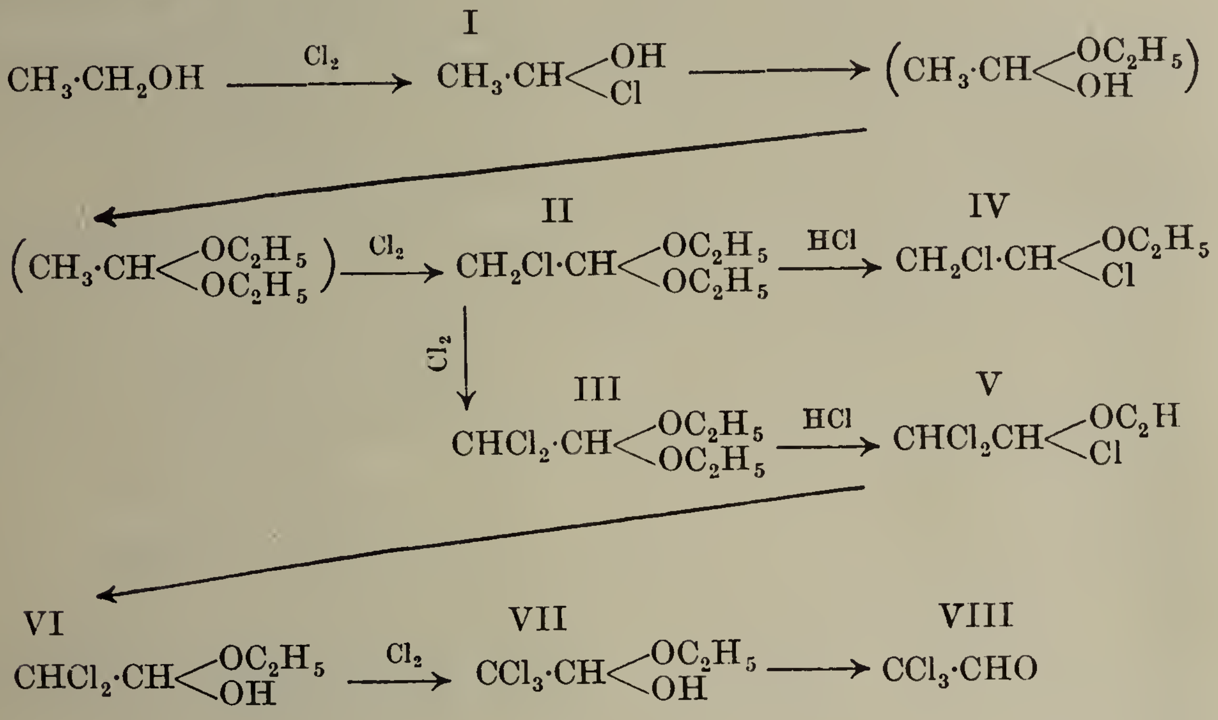
$$\underset{\text{Ricinoleic acid.}}{C_{18}H_{34}O_3} \longrightarrow \underset{\text{Undecenoic acid.}}{C_{10}H_{19}COOH} + \underset{\text{Œnanthal.}}{CH_3(CH_2)_5CHO}$$

A number of high molecular aldehydes occur in essential oils, *e.g.* n-*nonaldehyde* in Rose-oil (Ber. **33**, 2302), n-*decaldehyde* in orange-peel oil and acacia oil (J. pr. Chem. [2], **68**, 235), *lauraldehyde* in oil of silver-fir (C. 1904, I. 1264).

1. HALOGEN SUBSTITUTION PRODUCTS OF THE SATURATED ALDEHYDES

Trichloroacetaldehyde, *Chloral*, $CCl_3{\cdot}CHO$, which was discovered in 1832 by Liebig while engaged in studying the action of chlorine on alcohol (Ann. **1**, 182), is the most important of these compounds.

Fritsch considered that chlorine acts on alcohol to produce at first monochloroalcohol or aldehyde chlorhydrin (I). Alcohol and hydrochloric acid convert this, through the aldehyde alcoholate, into acetal. Neither substance can be isolated. Obviously acetal is chlorinated too easily to mono- and dichloroacetal (II and III). These two compounds, under the influence of hydrochloric acid, pass into dichloro- and trichloro-ether (IV and V). Water changes the latter to dichloroacetaldehyde alcoholate (VI), which is converted by chlorine into chloral alcoholate. Sulphuric acid decomposes the latter into alcohol and chloral (VIII) (Ann. **279**, 288 : C. 1897, I. 635, 801 : compare also the chlorination of *iso*butyl alcohol, Ber. **27**, R. 507).



$$CH_3\cdot CH_2OH \xrightarrow{Cl_2} \overset{\text{I}}{CH_3\cdot CH{<}^{OH}_{Cl}} \longrightarrow \left(CH_3\cdot CH{<}^{OC_2H_5}_{OH}\right)$$

$$\left(CH_3\cdot CH{<}^{OC_2H_5}_{OC_2H_5}\right) \xrightarrow{Cl_2} \overset{\text{II}}{CH_2Cl\cdot CH{<}^{OC_2H_5}_{OC_2H_5}} \xrightarrow{HCl} \overset{\text{IV}}{CH_2Cl\cdot CH{<}^{OC_2H_5}_{Cl}}$$

$$\downarrow Cl_2$$

$$\overset{\text{III}}{CHCl_2\cdot CH{<}^{OC_2H_5}_{OC_2H_5}} \xrightarrow{HCl} \overset{\text{V}}{CHCl_2CH{<}^{OC_2H}_{Cl}}$$

$$\overset{\text{VI}}{CHCl_2\cdot CH{<}^{OC_2H_5}_{OH}} \xrightarrow{Cl_2} \overset{\text{VII}}{CCl_3\cdot CH{<}^{OC_2H_5}_{OH}} \longrightarrow \overset{\text{VIII}}{CCl_3\cdot CHO}$$

Chloral hydrate, dichloroacetic ester, trichloro-ethyl alcohol (Ber. **26**, 2756), and ethylene monochlorhydrin are by-products in the manufacture of chloral. (Private communication from Anschütz and Stiepel.)

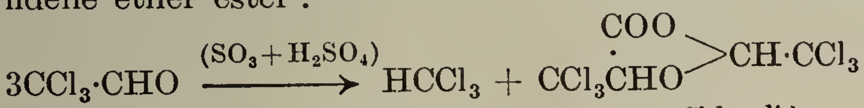
Chloral is an oily, pungent-smelling liquid, b.p. 97°, D_0 1·541. When kept for some time it passes into a solid polymer.

Chloral shows greater tendency than acetaldehyde to form addition compounds at the C : O linkage. Like acetaldehyde, it not only combines with acetic anhydride, the alkali bisulphites, ammonia and hydrocyanic acid, but also with water, alcohol, hydroxylamine, formamide—four substances with which acetaldehyde is incapable of uniting.

The following reactions of chloral should also be observed : (1) The alkalis break it down into chloroform and alkali formates :

$$CCl_3CHO + KOH = CHCl_3 + H\cdot CO_2K$$

(2) fuming sulphuric acid condenses it to chloralide (*q.v.*), trichlorolactic trichloroethylidene ether ester :



$$3CCl_3\cdot CHO \xrightarrow{(SO_3+H_2SO_4)} HCl_3 + \begin{matrix}COO\\ \cdot\\ CCl_3CHO\end{matrix}{>}CH\cdot CCl_3$$

Chloralide.

(3) potassium cyanide changes it to dichloroacetic ethyl ester (*q.v.*).

Trichloroethyl alcohol, CCl_3CH_2OH, is formed by the biochemical reduction of chloral by yeast. Its urethane is used as a hypnotic under the name *voluntal* (Ber. **56**, 2283).

Chloral hydrate, *Trichloroethylidene glycol,* $CCl_3\cdot CH(OH)_2$, m.p. 57°, b.p. 96–98°, results from the union of chloral with water. It is technically prepared on a large scale. It consists of large monoclinic prisms. Its vapour dissociates into chloral and water. Chloral hydrate dissolves readily in water, possesses a peculiar odour and a sharp, biting taste ; when taken internally it produces sleep, a fact which was discovered in 1869 by Liebreich (Ber. 2, 269). It is excreted in urine after administration as *urochloralic acid* (*q.v.*). Concentrated sulphuric acid resolves the hydrate into water and chloral. It reduces ammoniacal silver solutions and when oxidized with nitric acid yields trichloroacetic acid.

Chloral hydrate is the first example of a body which, contrary to the rule, contains two hydroxyl groups attached to the same carbon atom, without the occurrence of the immediate spontaneous cleavage of water.

Other halogen Substitution Products of Acetaldehyde.—**Dichloroacetaldehyde,** b.p. 88–90°, results from the action of concentrated H_2SO_4, or better, benzoic anhydride (Ber. **40**, 217), on dichloroacetal, $CHCl_2\cdot CH(OC_2H_5)_2$ (p. 242). *Dichloroacetaldehyde hydrate,* $CHCl_2\cdot CH(OH)_2$, m.p. 57°, b.p. 120°.

Monochloroacetaldehyde, b.p. 85°, is formed whem monochloroacetal (p. 242) is distilled with anhydrous oxalic acid. It polymerizes very readily (Ber. **15**, 2245).

Tribromoaldehyde, *Bromal,* $CBr_3\cdot CHO$, b.p. 172–173°, is perfectly analogous to chloral. Heated with alkalis, bromal breaks up into bromoform, $CHBr_3$, and a formate.

Bromal hydrate, $CBr_3CH(OH)_2$, m.p. 53°: *Bromal alcoholate,* $CBr_3CH(OH)\text{-}(O\cdot C_2H_5)$, m.p. 44°.

Dibromoacetaldehyde, b.p. 142°, is obtained by the bromination of paraldehyde.

Dibromoacetaldehyde hydrate, $CHBr_2CH(OH)_2$, m.p. 59°, is prepared by the addition of HBrO to acetylene (C. 1900, II, 29).

Bromoacetaldehyde, b.p. 80–105°, is produced from monobromoacetal.

Iodoacetaldehyde, $CH_2I\cdot CHO$, is made by acting on aldehyde with iodine and iodic acid. It is an oily liquid, which decomposes at 80° (Ber. **22**, R. 561).

The three chloro- (or bromo-) acetaldehydes may be considered the chlorides of the following hydroxy compounds:

$CH_2Cl\cdot CHO$, Chloroacetaldehyde.	$CH_2(OH)\cdot CHO$, Glycollic aldehyde.
$CHCl_2\cdot CHO$, Dichloroacetaldehyde.	$CHO\cdot CHO$, Glyoxal.
$CCl_3\cdot CHO$, Trichloroacetaldehyde.	$CO_2H\cdot CHO$, Glyoxylic acid.

Chlorine Substitution Products of the Higher Aldehydes:

β-Chloropropionic aldehyde, $CH_2Cl\cdot CH_2\cdot CHO$, m.p. 35°, from acrolein, $CH_2{=}CH\cdot CHO$, and hydrochloric acid.

β-Chlorobutyraldehyde, $CH_3\cdot CHCl\cdot CH_2\cdot CHO$, m.p. 96°, is produced from crotonaldehyde, $CH_3\cdot CH : CH\cdot CHO$, by the addition of HCl.

αα*β*-Trichlorobutyraldehyde, *Butyl chloral,* $CH_3\cdot CHCl\cdot CCl_2\cdot CHO$, b.p. 163–165°.

Butyl chloral hydrate, $CH_3CHCl\cdot CCl_2\cdot CH(OH)_2$, m.p. 78°, is formed from α-chlorocrotonaldehyde and Cl_2. Alkalis decompose it into formic acid, potassium chloride, and dichloropropylene, $CH_3\cdot CCl : CHCl$. It is converted, by nitric acid, into trichlorobutyric acid. When taken into the system it appears in the urine as *urobutylchloralic acid* (*q.v.*).

The relations of these three chlorinated aldehydes to the unsaturated aldehydes, from which they are formed by the addition of HCl or Cl_2, and to the acids which they yield on oxidation, are shown in the following table:—

$$\begin{array}{ccccc}
CH_2{=}CH\cdot CHO & \xrightarrow{HCl} & CH_2Cl\cdot CH_2\cdot CHO & \xrightarrow{HNO_3} & \overset{\beta}{C}H_2Cl\cdot\overset{\alpha}{C}H_2\cdot CO_2H. \\
\text{Acrolein.} & & \beta\text{-Chloropropionaldehyde.} & & \beta\text{-Chloropropionic acid.} \\
CH_3\cdot CH{=}CH\cdot CHO & \xrightarrow{HCl} & CH_3\cdot CHCl\cdot CH_2CHO & \longrightarrow & CH_3\cdot CHCl\cdot CH_2\cdot CO_2H. \\
\text{Crotonaldehyde.} & & \beta\text{-Chlorobutylaldehyde.} & & \beta\text{-Chlorobutyric acid.} \\
CH_3\cdot CH{=}CCl\cdot CHO & \xrightarrow{Cl_2} & CH_3\cdot CHCl\cdot CCl_2\cdot CHO & \longrightarrow & CH_3\cdot CHCl\cdot CCl_2\cdot CO_2H \\
\alpha\text{-Chlorocrotonaldehyde.} & & \text{Butylchloral.} & & \text{Trichlorobutyric acid.}
\end{array}$$

Tetrabromobutyric aldehyde, $CH_2Br\cdot CHBr\cdot CBr_2CHO$, m.p. 64°, b.p. 146°/13 mm., is prepared from paraldehyde and excess of bromine, with the intermediary production of crotonaldehyde. It does not form a hydrate, and is decomposed by alkalis into formic acid, bromopropargyl bromide, $CH_2Br\cdot C \vdots CBr$, and other bodies (C. 1905, II. 392: 1907, I. 1180).

ALDEHYDE PEROXIDES

Formaldehyde peroxide, *Dihydroxymethyl peroxide,* $HOCH_2{\cdot}O{\cdot}O{\cdot}CH_2OH$, is formed by the slow combustion of ethyl ether (Ber. **18**, 3343). It is obtained pure by the action of an ethereal solution of formaldehyde on an ethereal solution of hydrogen peroxide (see Proc. Roy. Soc. **90** [A], 492). It forms colourless crystals, m.p. 63° (Ann. **431**, 306). By the action of ammonia it yields hexaoxymethylenediamine, hexamethylenetriperoxydiamine, $N(CH_2O{\cdot}OCH_2)_3N$, which can also be easily prepared by the action of a solution of formaldehyde on ammonium sulphate dissolved in 3 per cent. hydrogen peroxide. The dry substance explodes as violently as diazobenzene nitrate on being heated, by friction or by a blow (Ber. **33**, 2486).

Acetaldehyde peroxide, *Dihydroxyethyl peroxide,* $(CH_3CHOH{\cdot})O_2$, is similarly prepared. It is an oil, appreciably less stable than the formaldehyde derivative (Ann. **431**, 314).

Dichloral peroxide hydrate, $CCl_3CH{<}\begin{matrix}O & \text{——} & O \\ OH & & HO\end{matrix}{>}CH{\cdot}CCl_3$, m.p, 122°, is prepared from chloral and H_2O_2 in an ether solution or potassium persulphate in sulphuric acid (Ber. **33**, 2481).

Aldehyde peroxides of the general formula $R{\cdot}CHO_2$ are obtained by the action of ozone on the aldehydes. They isomerize to the corresponding acid on heating (Ann. **374**, 321).

2. ETHERS AND ESTERS OF THE ALDEHYDE HYDRATES

As already mentioned, the aldehydes can be regarded as the anhydrides of the usually non-existent αα-glycols, $R{\cdot}CH(OH)_2$. These hydrates can generally only be isolated when derived from an aldehyde such as chloral which contains several halogen atoms. The mono-alkyl ethers of these hydrates (the *alcoholates*) are equally unstable, but the dialkyl ethers or *acetals* are stable bodies readily formed from all aldehydes.

$R{\cdot}CH(OH)_2$	$R{\cdot}CH(OH){\cdot}OR'$	$R{\cdot}CH(OR')_2$
Aldehyde hydrates.	Aldehyde alcoholates.	Acetals.

A. Alcoholates

Alcoholates only exist as addition products of alcohol with halogen substitution products of the aldehydes. In this they resemble the aldehyde hydrates which are only stable when a sufficient number of hydrogen atoms have been replaced by halogens.

Chloral alcoholate, $CCl_3CH{<}\begin{matrix}OH \\ OC_2H_5\end{matrix}$, m.p. 65°, b.p. 114°, is the main product from the action of chlorine on alcohol (p. 239). It is also formed by treatment of chloral or chloral hydrate with alcohol. Water changes it slowly into chloral hydrate (Ber. **28**, R. 1013). *Chloral dimethylethylcarbinolate,* $CCl_3CH(OH){\cdot}OC(CH_3)_2C_2H_5$, is prepared from chloral and amylene hydrate (p. 148), or chlorine, amylene and hydrochloric acid (C. 1900, II. 1167). *Further chloral alcoholates,* see C. 1908, I. 1561.

Bromal alcoholate, $CBr_3{\cdot}CH(OH){\cdot}OEt$, m.p. 44°.

B. Acetals

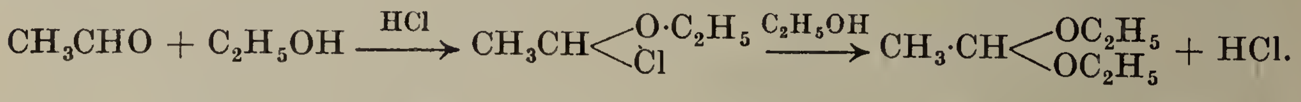
Acetals are produced (1) when alcohols are oxidized with MnO_2 and H_2SO_4. The aldehyde formed at first unites with alcohol with the simultaneous separation of water :

$$3CH_3{\cdot}CH_2OH \xrightarrow{O} CH_3CH(O{\cdot}C_2H_5)_2 + 2H_2O.$$

(2) When aldehydes are heated with the alcohols alone to 100° ; and from trioxymethylene and alcohols on the addition of ferric

chloride (1–4%) (Ber. **27**, R. 506), or syrupy phosphoric acid (C. 1899, I. 910).

(3*a*) By the action of gaseous HCl on a mixture of alcohol and aldehyde, a chlorhydrin (see Ethylene glycol) being the first product:



$$CH_3CHO + C_2H_5OH \xrightarrow{HCl} CH_3CH{<}\begin{smallmatrix}O{\cdot}C_2H_5\\ Cl\end{smallmatrix} \xrightarrow{C_2H_5OH} CH_3{\cdot}CH{<}\begin{smallmatrix}OC_2H_5\\ OC_2H_5\end{smallmatrix} + HCl.$$

(3*b*) More conveniently, by the action of 1% alcoholic hydrochloric acid on aldehyde (Ber. **31**, 545).

(4) By the action of metallic alcoholates on the corresponding chlorides, bromides and iodides.

(5) By the action of aldehydes on orthoformic ester or hydrochloric acid, formimido-ether and alcohol, *i.e.* on nascent orthoformic ester. This method is also employed for the preparation of acetals of the ketones (Ber. **31**, 1010: **40**, 3301).

On heating the acetals with alcohols, the higher alkyls are replaced by the lower (Ann. **225**, 265: C. 1901, I. 1146). When the acetals are digested with aqueous hydrogen chloride they are resolved into their constituents. They dissolve readily in alcohol and in ether, but with difficulty in water.

The acetals are considerably more stable towards alkalis than the aldehydes, and are mainly employed in those changes where aldehydes would be resinified or condensed.

Methylal, *Methylene dimethyl ether, Formal,* $CH_2(OCH_3)_2$, b.p. 42°, D. =0·855, is an excellent solvent for many carbon compounds. *Methylene diethyl ether, Diethyl formal,* $CH_2(OC_2H_5)_2$, b.p. 89°. For the higher methylals see Ber. **20**, R. 553; **27**, R. 507. *Dichloromethylal,* $CH_2(OCH_2Cl)_2$, b.p. 166°, is obtained from the interaction of paraformaldehyde and dichloromethyl ether, $O(CH_2Cl)_2$; and also from a formaldehyde solution and HCl (Ann. **334**, 1). With sodium methoxide and ethoxide it yields respectively *dimethoxymethylal,* b.p. 107°, and *diethoxymethylal,* b.p. 140°, having the general formula $CH_2(OCH_2OR)_2$ (C. 1904, II. 416, 1906, II. 226).

Ethylidene dimethyl ether, acetaldehyde dimethyl acetal, $CH_3CH(OCH_3)_2$, b.p. 64°.

Acetal, *Ethylidene diethyl ether,* $CH_3CH(OC_2H_5)_2$, b.p. 104°, $D_{20} = 0{\cdot}8314$, is produced in the process of brandy distillation. It is quite stable towards the alkalis, whilst dilute acids readily break it down into aldehyde and alcohol (Ber. **16**, 512).

Halogen Derivatives of Acetal.—*Monochloroacetal,* $CH_2Cl{\cdot}CH(OEt)_2$, b.p. 157°, *dichloroacetal,* $CHCl_2{\cdot}CH(OEt)_2$, b.p. 183–184°, and *trichloroacetal,* $CCl_3{\cdot}CH(OEt)_2$, b.p. 197°, can be obtained by the chlorination of acetal, but all are more readily prepared by the action of chlorine on alcohol under suitable conditions of cooling (Ann. **279**, 300).

Monobromoacetal, $CH_2BrCH(OC_2H_5)_2$, b.p. 170°, is produced from acetal, bromine, and $CaCO_3$; or from paraldehyde, bromine, and alcohol (Ber. **25**, 2551: C. 1905, I, 1218: 1907, I. 1180). Sulphuric acid decomposes the halogen acetals into alcohol and halogen-aldehydes (p. 240). *Iodoacetal,* $I{\cdot}CH_2{\cdot}CH(OC_2H_5)_2$, b.p. 100°/10 mm. (Ber. **30**, 1442).

Butylchloralacetal, $CH_3CHCl{\cdot}CCl_2CH(OC_2H_5)_2$, b.p. 123°/20 mm. (C. 1907, I. 152).

The polymeric modifications of aldehyde are closely related to the acetals, and result from an acetal-like union of similar molecules (p. 236). If molecules of different aldehydes take part in the reaction, there are obtained compounds similar to those formed by polymeric aldehydes; chloral and formaldehyde, with concentrated H_2SO_4 give Hexachlorodimethyltetroxan, $CCl_3CH{<}\begin{smallmatrix}O{\cdot}CH_2{\cdot}O\\ O{\cdot}CH_2{\cdot}O\end{smallmatrix}{>}CHCCl_3$ and Hexachlorodimethyltrioxan, $CCl_3CH{<}\begin{smallmatrix}O{\cdot}CH_2{\cdot}O\\ O\end{smallmatrix}{>}CHCl_3$ (Ber. **33**, 1432).

C. Aldehyde Dihalides and Halogenohydrins

The aldehyde dihalides, $R \cdot CHX_2$, and the aldehyde halogenohydrins, $R \cdot CH(OH) \cdot X$, can be regarded as the di- and mono-halide esters of the non-existent αα-glycols, or aldehyde hydrates, $R \cdot CH(OH)_2$. The ethers of the halogenohydrins, $R \cdot CH(OR') \cdot X$, can also be regarded as α-halogen substitution products of the ethers, $R \cdot CH_2 \cdot OR'$.

1. **Aldehyde Dihalides,** $R \cdot CHX_2$.—The dichloro-compounds are readily produced by heating aldehydes with phosphorus pentachloride, and re-form the aldehyde when heated with water at 100°.

Name.	Formula.	M.P.	B.P.	D.
Methylene chloride .	CH_2Cl_2	—	41°	1·37 (0°)
Methylene bromide .	CH_2Br_2	—	98°	2·54 (0°)
Methylene iodide .	CH_2I_2	+ 4°	181°	3·28 (15°)
Ethylidene chloride .	CH_3CHCl_2	—	60°	1·17 (20°)
Ethylidene bromide .	CH_3CHBr_2	—	110°	2·02 (20°)
Ethylidene iodide . .	CH_3CHI_2	—	127°/171 mm.	2·84 (0°)
Propylidene chloride .	$CH_3 \cdot CH_2CHCl_2$	—	86°	1·16 (14°)

Methylene chloride is formed from CH_3Cl and Cl, by the reduction of chloroform by means of zinc in alcohol, and from trioxymethylene and PCl_5.

Methylene bromide results on heating CH_3Br with bromine to 180°, and by the action of trioxymethylene on aluminium bromide, or phosphorus pentabromide.

Methylene iodide is produced when iodoform is reduced with HI, or better, with arsenious acid and sodium hydroxide (*Klinger*). It is characterized by a high specific gravity. Chlorine and bromine change it to methylene chloride and bromide. Mercury produces the derivative ICH_2HgI (C. 1901, I. 1264). Heated with copper in a sealed tube it yields ethylene (p. 102).

Ethylidene chloride is produced (1) from aldehyde by the action of PCl_5, (2) from vinyl bromide by means of hydrogen bromide, and (3) by treating copper acetylide with concentrated hydrochloric acid (Ann. **178**, 111). Ethylene (p. 102) is produced by the action of sodium.

Ethylidene bromide is obtained by the action of PCl_3Br_2 on aldehyde (Ber. **5**, 289).

Ethylidene iodide is obtained from acetylene and hydriodic acid (Ber. **28**, R. 1014).

2. **Aldehyde Halogenohydrins.**—These are only known as their ethers, the α-halogen ethers, $R \cdot CH(OR') \cdot X$. The latter are obtained by the action of alcohols and halogen acids on the aldehydes, and are readily converted by the further action of alcohols or alkoxides into the dialkyl ethers, acetals.

Monochloromethyl ether, $CH_2Cl \cdot OMe$, b.p. 59·2°, D_4^{15} 1·0771. *Monochloromethyl ethyl ether*, $CH_2Cl \cdot OEt$, b.p. 83°, D_4^{15} 1·0188. *Monochloromethyl propyl ether*, $CH_2Cl \cdot O \cdot C_3H_7$, b.p. 109°, and higher homologues are obtained from trioxymethylene, hydrochloric acid and the corresponding alcohol (Ber. **38**, 1383 : Ann. **334**, 49 : C. 1912, II. 1266).

They are highly reactive bodies ; with *water* they regenerate formaldehyde ; with *formates* and *acetates* they yield ether-esters of the type $HCOOCH_2OR$; with *magnesium alkyl halides* they give simple ethers (p. 155) ; with magnesium in presence of ketones or carboxylic esters or magnesium-organic compounds such as $ROCH_2MgX$ (p. 366), they form ethers of the ethylene glycols, $R''R'$-$C(OH)CH_2OR$, or diethers of the glycerols, $R'C(OH)(CH_2OR)_2$; with *mercury* or *copper cyanides* they are converted into nitriles of alkoxyl glycollic acid $NC \cdot CH_2OR$ (C. 1907, I. 400, 871). They yield hexamethylenetetramine with ammonia (p. 248), and form quaternary ammonium salts, $ClR_3NCH_2OCH_3$, with tertiary amines.

Monobromomethyl ether, b.p. 87° ; D_4^{15} 1·6065. *Monoiodomethyl ether*, b.p. 124° ; D_{16} = 2·0249 (Ber. **26**, R. 933).

α-Monochloroethyl ether, $CH_3CHCl \cdot O \cdot CH_2CH_3$, b.p. 98°, isomeric with ethylene chlorhydrin ethyl ether, $ClCH_2CH_2 \cdot O \cdot C_2H_5$, is produced by the chlorination of ether, and by saturating a mixture of aldehyde and alcohol with hydrochloric acid, into which substances it is again resolved by water. *α-Monobromoethyl ether*, b.p. 105° (Ber. **18**, R. 322).

Tetrachloroethyl ether, $CCl_3 \cdot CHCl \cdot OEt$, b.p. 189°, from chloral alcoholate and PCl_5 (J.A.C.S. **31**, 410).

3. *sym.-αα′*-**Dihalogen alkyl ethers**, *Ethers of the aldehyde halohydrins* result from the action of the halogen acids on trioxymethylene (C. 1900, I. 1122: 1901, II. 26: Ann. **334**, 1).

sym.-*Dichloromethyl ether*, $(CH_2Cl)_2O$, b.p. 105°, $D = 1 \cdot 315$, is also obtained, together with dichloromethylal from trioxymethylene and PCl_3. sym.-*Dibromomethyl ether*, b.p. 150°. sym.-*Diiodomethyl ether*, b.p. 218°.

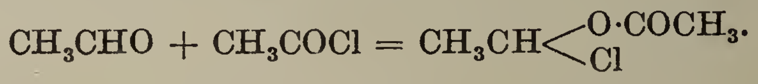
αα-Dichloroethyl ether, $(CH_3 \cdot CHCl)_2O$, b.p. 116°.

D. Carboxylic Esters of the Aldehyde Hydrates

The carboxylic esters of the alkylidene glycols, $R \cdot CH(OR')_2$, are formed (1) from aldehydes and acid anhydrides:

$$CH_3CHO + (CH_3CO)_2O = CH_3CH(OCOCH_3)_2.$$

(2) From aldehydes and acid chlorides:



$$CH_3CHO + CH_3COCl = CH_3CH<\begin{matrix}O \cdot COCH_3.\\ Cl\end{matrix}$$

(3) From the corresponding chlorides, bromides, and iodides by the action of silver salts:

$$CH_2I_2 + 2CH_3CO_2Ag = CH_2(OCOCH_3)_2 + 2AgI.$$

When boiled with water these esters break down into aldehydes and acids.

Methylene diacetate, $CH_2(OCOCH_3)_2$, b.p. 170°. For higher homologues see C. 1902, II. 933; 1903, II. 656. *Ethylidene diacetate*, $CH_3CH(O \cdot COCH_3)_2$, b.p. 169°.

Chloral diacetate, $CCl_3 \cdot CH(OCOCH_3)_2$, b.p. 221°. Bromal diacetate, m.p. 76°.

Monochloromethyl acetate and *monobromomethyl acetate*, $Br \cdot CH_2OCOCH_3$, b.p. 130°, are prepared from trioxymethylene and acetyl chloride or bromide (C. 1901, II. 396). *α-Monochloroethyl acetate*, $CH_3CHCl \cdot OCOCH_3$, b.p. 121·5°, is the parent substance for the preparation of ether-esters and mixed ethers. *α-Chloroethyl propionate*, b.p. 134–136°. Silver propionate with the first chlorhydrin forms the same *aceto-ethylidine propionate*, $CH_3COO \cdot CH(CH_3)OCOC_2H_5$, b.p. 178·6°, as silver acetate with the second chlorhydrin. These facts argue for the equivalence of the carbon valencies (Geuther, Ann. **225**, 267).

Chloral acetyl chloride, $CCl_3CHCl(OCOCH_3)$, b.p. 193°. *Bromal acetyl chloride* (C. 1900, II. 811). *Chloral ethyl acetate*, $CCl_3 \cdot CH(OC_2H_5)O \cdot COCH_3$, b.p. 198° (C. 1901, I. 930).

E. Aldehyde-Bisulphites and Aldehyde Sulphoxylates

Aldehydes in aqueous solution absorb sulphurous acid with evolution of heat (Ber. **38**, 1076: C. 1904, II. 54). The sulphur dioxide is driven off by heat. On the other hand, aldehydes unite with bisulphites to form compounds of the general formula, $R \cdot CHOH \cdot SO_3M$, which usually crystallize well, and serve to characterize the aldehydes. These compounds are known as the aldehyde bisulphites.

According to Raschig, these compounds are to be regarded as α-hydroxysulphonic acids, $R \cdot CH(OH) \cdot SO_2ONa$, in which the sulphur is directly linked to carbon (*Raschig* and *Prahl*, Ber. **59**, 859, 2025: Ann. **448**, 265). Objection has been taken to this sulphonic acid formulation, largely on account of the lability of these compounds towards acids and alkalis, whereas the ordinary sulphonic acids are stable under identical conditions, and also because the β-hydroxypropanesulphonic acid obtained from propane-ββ-disulphonic acid is different from " acetone bisulphite " (Ber. **59**, 1695, 2341). Raschig has replied to this criticism of Schroeter's that the lability of the sulphonic acid group is caused by the presence of an ·OH group on the same carbon atom (Ber. **61**, 179). The investigation of the X-ray absorption spectra of these compounds supports Raschig's views (Stelling) (*cf.* also the observations of *Bazlen*, Ber. **60**, 1470).

The aldehydes also yield " bisulphite compounds " when treated with neutral sulphites, an equivalent amount of alkali being liberated. This can be titrated for quantitative determination of aldehydes (C. 1904, I. 1176, 1457):

$$R{\cdot}CHO + Na_2SO_3 + H_2O \longrightarrow R{\cdot}CH(OH){\cdot}SO_3Na + NaOH.$$

The aldehyde bisulphites show the following reactions:

(1) They are easily decomposed by hydrochloric acid or alkalis, regenerating the aldehyde;

(2) They are easily transformed by aqueous solutions of alkali cyanides, forming aldehyde cyanhydrins or α-hydroxynitriles (Ber. **37**, 4060: **38**, 213).

$$HO{\cdot}CH_2{\cdot}SO_3K + KCN = HOCH_2CN + K_2SO_3;$$

(3) They are converted by ammonia or amines into alkylidene amino-sulphites (Ber. **37**, 4075: **38**, 1077):

$$HO{\cdot}CH_2{\cdot}SO_3Na + NH_3 = NH_2{\cdot}CH_2{\cdot}SO_3Na + H_2O;$$

(4) When reduced by zinc dust and acetic acid, they yield aldehyde sulphoxylates (Ber. **38**, 1073: C. 1905, II. 1752). According to Bazlen (Ber. **60**, 1470) the sulphoxylates are to be regarded as salts of hydroxysulphinic acids, similarly to Raschig's view of the bisulphite compounds.

$$R{\cdot}CHOH{\cdot}SO_3Na + 2H \longrightarrow R{\cdot}CHOH{\cdot}SO_2Na + H_2O.$$

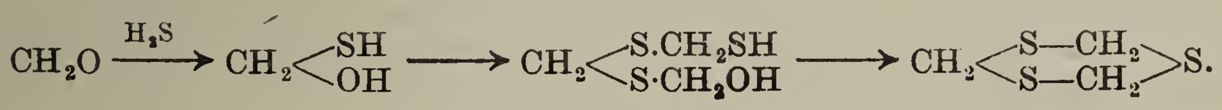
Formaldehyde sulphoxylate, $HOCH_2{\cdot}OSONa + 2H_2O$, withstands the action of alkalis better than formaldehyde bisulphite. It forms small rhombic prisms (C. 1905, I. 795). A finely crystallizing double compound of formaldehyde sulphoxylate and formaldehyde bisulphite (Ber. **38**, 2290) may be prepared from formaldehyde and sodium hydrosulphite, $Na_2S_2O_4$. This body, known under the name of *Rongalite*, is of technical importance in the dyeworks where, in discharge work, the reducing action of sodium hydrosulphite is developed at a raised temperature and then only acts on the azo-dyestuffs, indigo, etc., without attacking the fibre. Rongalite can be split up into its constituent compounds by fractional crystallization. Sulphoxylates react with amines similarly to the aldehyde bisulphites.

3. SULPHUR DERIVATIVES OF THE SATURATED ALDEHYDES

In this class are (A) the thioaldehydes, their polymeric modifications and their sulphones; (B) the mercaptals or thioacetals, with their sulphones; and (C) the hydroxysulphonic and disulphonic acids of the aldehydes.

A. Thioaldehydes, Polymeric Thioaldehydes and their Sulphones

The simple thioaldehydes are not well known, whilst the polymeric thioaldehydes are more accessible. All of them can be regarded as the alkyl derivatives of polymeric trithioformaldehyde (trithiomethylene) discovered by *A. W. Hofmann*. They are formed when the aldehydes are acted on with H_2S and HCl. The H_2S adds itself to the C=O-group of the aldehydes, and hydroxy-hydrosulphides result, from which the trithioaldehydes arise:



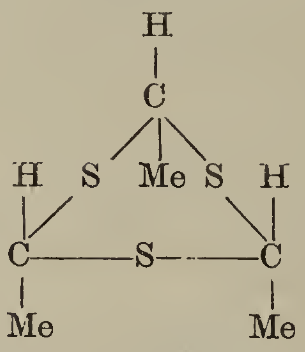
$$CH_2O \xrightarrow{H_2S} CH_2{<}\begin{array}{l}SH\\OH\end{array} \longrightarrow CH_2{<}\begin{array}{l}S.CH_2SH\\S{\cdot}CH_2OH\end{array} \longrightarrow CH_2{<}\begin{array}{l}S{-}CH_2\\S{-}CH_2\end{array}{>}S.$$

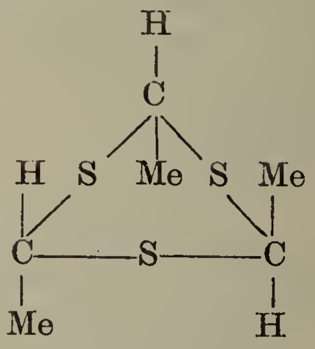
The trithioaldehydes are odourless solids, whereas the simple thioaldehydes and their mercaptan-like transposition products possess a persistent, disagreeable odour.

The trithioaldehydes are oxidized by hydrogen peroxide or potassium permanganate to sulphide-sulphoxides, trisulphoxides, sulphide-sulphones (J. pr. Chem. [2] **89**, 547) and finally into trisulphones. The molecular weight of the trithioaldehydes has been determined both by vapour density and by the lowering of the freezing point of their naphthalene solution. *Klinger* first proposed the structure for the trithioaldehydes which corresponds with the formula of paraldehyde and was proved correct by the oxidation of the trithioaldehydes to trisulphones.

The isomeric phenomena of the trithioaldehydes were considered by Baumann and Fromm to be due to their space-configurations (Ber. **24**, 1426).

Proceeding from the same considerations, which served Baeyer in his explanation of the isomerism of the hexamethylene derivatives (see Hexahydrophthalic acids), they distinguished α- or *cis*- and β- or *trans*-modifications. *Camps* represents the two trithioacetaldehydes in the following way:


α or *cis*-form.


β- or *trans*-form.

The three alkyl groups are on the same side of the ring in the α- or *cis*-form and on the opposite sides in the β- or *trans*-form.

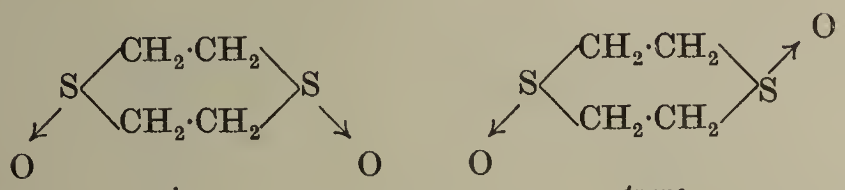
Only one disulphone-sulphide corresponds with the *cis*-modification, whilst *two* stereoisomeric disulphone-sulphides take the *trans*-form.

Trithioformaldehydes.—α-*Trithioformaldehyde* (*Trimethylene trisulphide*) $(CH_2S)_3$, m.p. 216°, is obtained by heating formaldehyde sodium thiosulphate and hydrochloric acid together (J. pr. Chem. [2] **77**, 367). The intermediate formation of hydroxymethylthiosulphuric acid, $HOCH_2{\cdot}S{\cdot}SO_3H$, which then decomposes into the thioaldehyde and sulphuric acid, is probable (Ber. **40**, 865 : **47**, 306). On heating trithioformaldehyde with methyl iodide and methyl alcohol, trimethylsulphonium iodide is formed (see p. 174) (C. 1906, I. 649). By the prolonged action of concentrated hydriodic acid, the α- compound changes into the isomeric β-*trithioformaldehyde*, m.p. 247°, which readily reverts to the more stable low-melting α-form (J. pr. Chem. [2], 88, 50).

Trithioacetaldehydes.—α-*Trithioacetaldehyde*, m.p. 101°, b.p. 246–247°, and β-*trithioacetaldehyde* $[CH_3CHS]_3$, m.p. 125–126°, b.p. 245–248° ; at low temperatures the α-form predominates, but can be changed in considerable proportion into the β-form by the aid of catalysts such as iodine, zinc chloride, acetyl chloride, hydrochloric acid, etc. (Ber. **24**, 1457 ; C. 1905, II. 1720 : compare also C. 1904, II. 21).

Sulphoxides and Sulphones of the Trithioaldehydes

These are obtained from the trithioaldehydes by oxidation with hydrogen peroxide or permanganate. The trisulphones, and to a less extent, trimethylene trisulphoxide, possess an acidic character and are soluble in alkalis and alkali-carbonates. The hydrogen atoms in the methylene groups of trimethylene trisulphone are replaceable by metals, and by treatment of the sodium derivative with alkyl iodides, the hexaalkyl derivatives, identical with the oxidation products of the trithioketones, are formed. The stereoisomerism of the trithioaldehydes was said to be lost in their oxidation products (Ber. **26**, 2074 : **27**, 1667). However, recent work on the disulphoxide of diethylene disulphide shows that this substance exists in two stereoisomeric forms which can be represented as follows, and it is suggested that further investigation of the two trimethylene trisulphoxides (J. pr. Chem. [2] **85**, 339 : **89**, 547) may enable similar constitutions to be assigned to them (J.C.S. **1927**, 1798), the oxygen being united to sulphur by a semi-polar double bond (p. 31).



cis. *trans.*

Trimethylene trisulphone, $CH_2<\substack{SO_2—CH_2\\SO_2—CH_2}>SO_2$, *trimethylene disulphone sulphide*, $CH_2<\substack{SO_2\cdot CH_2\\SO_2\cdot CH_2}>S$, and *triethylidene trisulphone*, $[CH_3CHSO_2]_3$ m.p. above 340° (Ber. **25**, 248).

The two isomeric trithioacetaldehydes yield *triethylidene disulphone sulphide*, $CH_3\cdot CH\cdot<\substack{SO_2CH(CH_3)\\SO_2CH(CH_3)}>S$, m.p. 228–231°.

Thialdine, $CH_3\cdot CH<\substack{S\cdot CH(CH_3)\\S\cdot CH(CH_3)}>NH$, m.p. 43°, is produced by the action of NH_3 on α-trithioacetaldehyde (Ber. **19**, 1830), and of H_2S on aldehyde-ammonia (Ann. **61**, 2). It yields ethanedisulphonic acid (p. 248) by oxidation. *Methyl thialdine*, $(C_2H_4)_3S_2(NCH_3)$, m.p. 79° (Ber. **19**, 2378).

B. Mercaptals or Thioacetals and their Sulphones

The thioacetals, corresponding with the acetals (p. 241), are called *mercaptals*. They are formed (1) from alkyl iodides and alkali mercaptides; (2) by the action of HCl on the aldehydes and mercaptans. First an addition product is formed such as $CH_2(OH)SC_5H_{11}$, which with a second mercaptan molecule loses water and yields a mercaptal. It is possible, therefore, to prepare mercaptals containing two different alkyl groups (Ber. **36**, 296). They are oils with very unpleasant odours, and are oxidized by $KMnO_4$ to sulphones.

$$CH_2<\substack{S\cdot C_2H_5\\S\cdot C_2H_5}\xrightarrow{40}CH_2<\substack{SO_2\cdot C_2H_5\\SO_2\cdot C_2H_5}.$$

Methylene diethyl mercaptal, $CH_2(SC_2H_5)_2$, b.p. about 180°. *Ethylidene diethyl mercaptal, Dithioacetal*, $CH_3CH(SC_2H_5)_2$, b.p. 186°. *Propylidene diethyl mercaptal*, $CH_3CH_2CH(SC_2H_5)_2$, b.p. 198°.

In the **sulphones** of the mercaptals the methylene hydrogen (see above) is replaceable by alkali metals. Mono- and dialkylated sulphones can be prepared from these alkali derivatives. Again, the dialkylated sulphones may be obtained from the *mercaptoles* (p. 267); sulphonal belongs to this class.

Methylene diethyl sulphone, $CH_2(SO_2C_2H_5)_2$, m.p. 104°, is readily soluble in water and in alcohol. It is formed in the oxidation of orthothioformic ethyl ester (*q.v.*). It condenses with formaldehyde, forming methylene dimethenyl tetraethyl sulphone (Ber. **33**, 1120). *Methylene ethyl phenyl disulphone*, $CH_2(SO_2C_2H_5)(SO_2C_6H_5)$, m.p. 111° (Ber. **36**, 300). *Ethylidene diethyl sulphone*, $CH_3CH(SO_2C_2H_5)$, m.p. 75°, b.p. 320° with decomposition.

C. Hydroxysulphonic Acids and Disulphonic Acids of the Aldehydes

Hydroxymethanesulphonic acid, $CH_2(OH)SO_3H$, is formed together with hydroxymethanedisulphonic acid, $CH(OH)(SO_3H)_2$, and methanetrisulphonic acid, $CH(SO_3H)_3$, by the action of fuming sulphuric acid on methyl alcohol and subsequent boiling of the product with water. Boiling acids or alkalis have no effect on it (comp. p. 245).

Methionic acid, Methanedisulphonic acid, $CH_2(SO_3H)_2$, has long been known. It is produced when fuming sulphuric acid acts on acetamide, acetonitrile, lactic acid, etc. It is most conveniently made by saturating fuming sulphuric acid with acetylene, but *acetaldehyde disulphonic acid*, $CHO\cdot CH(SO_3H)_2$ is also largely formed. This latter acid can be completely decomposed by alkalis into formic and methionic acids :

$$\underset{\text{Acetylene.}}{CH:CH} \xrightarrow{O(SO_3H)_2} \underset{\text{Acetaldehyde disulphonic acid.}}{OCH{\cdot}CH(SO_3H_2)} \xrightarrow{H_2O} \underset{\text{Formic acid.}}{HO_2CH} + \underset{\text{Methionic acid.}}{CH_2(SO_3H)_2}$$

Methionic acid crystallizes in deliquescent needles, which are not decomposed by boiling nitric acid. *Barium salt*, $CH_2(SO_3)_2Ba + 2H_2O$, forms pearly leaflets dissolving with difficulty.

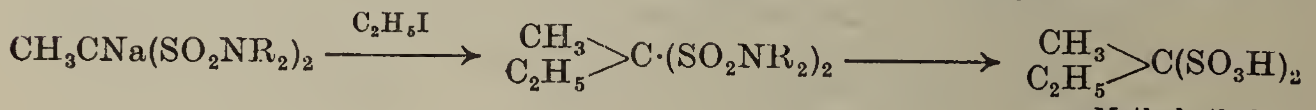
Methionic methyl ester, $CH_2(SO_3CH_3)_2$, m.p. 70°, b.p. 194–200°/16 mm. : *ethyl ester*, m.p. 29°, result from the action of silver methionate on alkyl iodides : easily hydrolysed by water. The esters are good alkylating agents. For additional salts and esters, see Ann. **418**, 191, 196.

Methionyl chloride, $CH_2(SO_2Cl)_2$, b.p. 135°/10 mm., $D._{15} = 1{\cdot}82$, is formed from methionic acid and phosphorus pentachloride. It reacts energetically with water or alcohol, regenerating methionic acid. With amines, especially those of the aromatic series, it forms amides.

Methionic anilide, $CH_2(SO_2NHC_6H_5)_2$, m.p. 193°, yields well-crystallizable or insoluble salts : $CH_2(SO_2NMC_6H_5)_2$. *Methionic diethylanilide*, $CH_2(SO_2N[C_2H_5]{\cdot}C_6H_5)_2$, m.p. 113°.

The esters, still better the dialkyl amides of methionic acid, react with potassium and sodium, evolving hydrogen and forming salts, $KCH(SO_3R)_2$ and $NaCH(SO_2NR_2)_2$ which readily undergo transformation with alkyl halides, acyl halides and carboxylic esters. As a result, *homologues of methionic acid* can be formed in the same way as malonic ester is caused to yield its homologues (*G. Schroeter*, Ann. **418**, 161 : Ber. **59**, 2341)

$$NaCH(SO_2NR_2)_2 \xrightarrow{C_2H_5I} C_2H_5CH(SO_2NR_2)_2 \longrightarrow \underset{\text{Ethyl methionic acid.}}{C_2H_5CH(SO_3H)_2}$$



$$CH_3CNa(SO_2NR_2)_2 \xrightarrow{C_2H_5I} \begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>C{\cdot}(SO_2NR_2)_2 \longrightarrow \begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>C(SO_3H)_2$$

Methyl ethyl methionic acid.

Ethane-αα-disulphonic acid, *Methylmethionic acid*, $CH_3CH(SO_3H)_2$ is also formed from thialdine (p. 247) by oxidation with permanganate (Ber. **12**, 682 : **21**, 1550).

4. NITROGEN-CONTAINING DERIVATIVES OF THE ALDEHYDES

A. Compounds derived from Ammonia and Alkylamines with Aldehydes

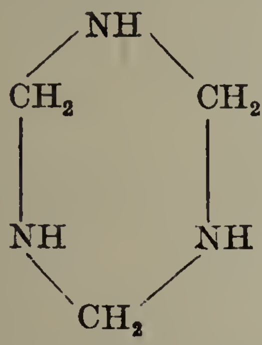
Ammonia combines directly with acetaldehyde and its higher homologues, forming " *aldehyde-ammonias* " or α-amino alcohols.

$$R{\cdot}CHO + NH_3 \longrightarrow R{\cdot}CH(OH){\cdot}NH_2.$$

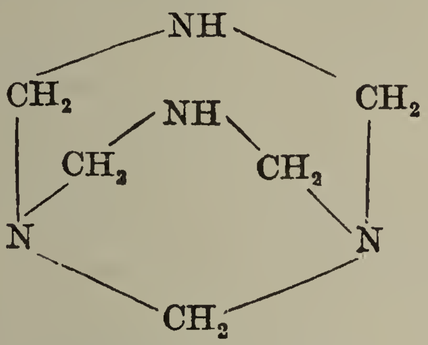
The aldehyde ammonias can be dehydrated to form *aldimines*, $R{\cdot}CH:NH$. With formaldehyde, on the other hand, it forms the compound hexamethylene tetramine, $(CH_2)_6N_4$, with elimination of water.

Hexamethylenetetramine, (*Hexamine, Urotropine*) is very much used in medicine as a urinary antiseptic. The antiseptic property is due to its hydrolysis, with formation of formaldehyde, in acid urine. It forms soluble compounds with uric acid, but is of little value in the treatment of gout.

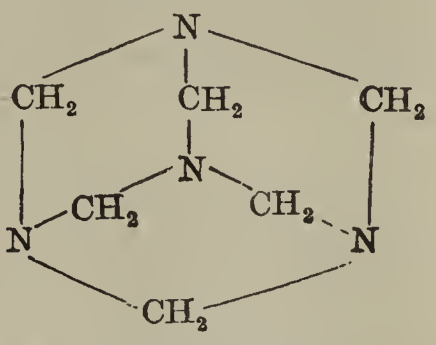
It is very soluble in water, and crystallizes from alcohol in brilliant rhombohedra. It sublimes without decomposition under reduced pressure. It is resolved into CH_2O and ammonia when distilled with sulphuric acid. It is a monacid base, but shows no reaction with litmus (Ber. **22**, 1929). Efforts have been made to ascertain its molecular weight by the analysis of its salts, by an approximation of its vapour density, and by the lowering of the freezing point of its aqueous solution (Ber. **19**, 1842 : **21**, 1570). Nitrous acid first converts hexamethylenetetramine into dinitrosopentamethylenetetramine, and this then into trinitrosotrimethylenetriamine. When it is considered that trimethylenetrimethyltriamine is formed by the interaction of methylamine and formaldehyde, it is obvious that the reaction must cease at this point, because the imide-hydrogen atoms have been replaced by methyl groups. Ammonia and formaldehyde yield at first trimethylene triamine, corresponding with trimethylenetrimethyltriamine, which reacts with, further, ammonia and formaldehyde, splits off water and becomes pentamethylenetetramine. The latter is converted by formaldehyde into hexamethylenetetramine. The following constitutional formulæ aim to represent this behaviour (comp. *Duden* and *Scharff*, Ann. **288**, 218 : see also C. 1898, I. 36):



Trimethylene triamine.



Pentamethylene tetramine.



Hexamethylene tetramine.

Hexamethylene tetramine forms addition compounds with bromine, iodine, iodoalkyls and iodine, mercuric iodide and iodine, chloral and bromal (C. 1898, II. 663 : 1900, I. 409):

$$(CH_2)_6N_4I_4, \quad (CH_2)_6N_4I_2{\cdot}CH_3I, \quad (CH_2)_6N_4I_2{\cdot}2HgI_2, \quad (CH_2)_6N_4{\cdot}CCl_3CHO + 2H_2O.$$

When heated with hydrochloric or acetic acid urotropine is decomposed respectively into formaldehyde and ammonia or into methylamine and CO_2 (C. 1906, I. 1088). Compare the formation of trimethylamine by heating formaldehyde with ammonium salts (p. 189).

Hydrogen peroxide reacts with hexamine in neutral solution to form the double compound, $(CH_2)_6N_4, H_2O_2$, but in acid solution forms hexaoxymethylenediamine (p. 241), which can also be produced by the action of ammonia on formaldehyde peroxide (Ber. **45**, 2571).

Aldehyde-ammonia, $CH_3CH(OH)NH_2$, m.p. 70–80°, is produced when dry ammonia gas is conducted into an ethereal solution of aldehyde, and consists of brilliant rhombohedra, dissolving readily in water. Acids resolve it into its components (p. 231):

$$CH_3{\cdot}CHO \xrightarrow{NH_3} CH_3{\cdot}CH(OH)NH_2 \xrightarrow{H_2SO_4} CH_3CHO + NH_4H{\cdot}SO_4.$$

When kept for a long time *in vacuo* over sulphuric acid, the original crystals gradually change into gleaming white ones of **ethylidenimine**, $(CH_3CH{=}NH)_3$, m.p. 85°, b.p. 123°. The *picrate*, recrystallized from alcohol, has the formula $(C_2H_5N)_3{\cdot}C_6H_2(NO_2)_3OH + C_2H_5OH$ (C. 1899, I. 420).

In contact with water it passes into amorphous *hydracetamide*, $C_6H_{12}N_2$. Sodium nitrite, added to a slightly acidified solution of aldehyde-ammonia, produces *nitrosoparaldimine*, $C_6H_{12}O_2(N{\cdot}NO)$, which by reduction yields *aminoparaldimine*, $C_6H_{12}O_2(N{\cdot}NH_2)$, and this in turn, by the action of dilute sulphuric acid, splits off hydrazine, $NH_2{\cdot}NH_2$ (Ber. **23**, 740). Paraldimine should be viewed as paraldehyde in which an oxygen atom has been replaced by the imino-group. Hydrogen sulphide changes aldehyde-ammonia to *thialdine* (p. 247), whilst with hydrocyanic acid it becomes the nitrile of α-aminopropionic acid (*q.v.*). A remarkable reaction occurs when aldehyde-ammonia acts on acetoacetic ester, resulting in the formation of 1,3,5-trimethyldihydropyridinedicarboxylic ester (Vol. II).

Hexaethylidenetetramine, $(CH_3CH)_6N_4$, m.p. 102°, with $6H_2O$, m.p. 96°, is obtained by heating aldehyde-ammonia with aqueous ammonia to 150° (C. 1900, I. 901).

Chloral-ammonia,  $CCl_3CH{<}^{NH_2}_{OH}$, m.p. 63°.

For the **chloralimides**, $(CCl_3{\cdot}CH:NH)_3$, and **dehydrochloralimides,** $C_6H_4Cl_9N_3$, consult Ber. **25**, R. 794 : **24**, R. 628. The isomerism of the former is very probably dependent upon the same causes as that of the polymeric thioaldehydes (p. 245).

Aldehyde bisulphites react with ammonia or alkylamines to form certain compounds, which can also be obtained from the aldimines and sodium bisulphite (Ber. **37**, 4087 : **38**, 1077). These were formerly regarded as sulphurous esters of the aldehyde ammonias, but on the analogy of the aldehyde bisulphites (see p. 244) are probably to be regarded as α-aminosulphonic acids.

Aminomethanesulphonic acid, $NH_2{\cdot}CH_2{\cdot}SO_3H$, forms crystals sparingly soluble in cold water. **Sodium diethylaminomethanesulphonate**, $NEt_2{\cdot}CH_2{\cdot}SO_3Na$, gives *tetraethylmethylenediamine* on warming with hydrochloric acid or sodium hydroxide, and *diethylaminomethyl acetate*, $NEt_2{\cdot}CH_2{\cdot}O{\cdot}COCH_3$, b.p. 81°/14 mm., with acetic anhydride. With aqueous potassium cyanide, it forms *diethylaminoacetonitrile*, $NEt_2{\cdot}CH_2{\cdot}CH$.

Compounds from Aldehydes and Alkylamines

The following bodies are produced when primary amines act on formaldehyde (Ber. **28**, R. 233, 381, 924 : **29**, 2110):

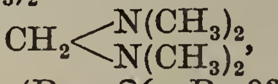
Methylmethyleneamine, $[CH_2{=}N{\cdot}CH_3]_3$, b.p. 166°; $D_{18\cdot7} = 0{\cdot}9215$.
Ethylmethyleneamine, $[CH_2{=}N{\cdot}C_2H_5]_3$, b.p. 207°; $D_{18\cdot7} = 0{\cdot}8923$.
n-*Propylmethyleneamine*, $[CH_2{=}N{\cdot}C_3H_7]_3$, b.p. 248°; $D_{18\cdot7} = 0{\cdot}880$.

The hydroiodides of methyl and ethylmethyleneamines are converted by heat into isomeric salts possessing the characteristics of quaternary ammonium salts, as is perhaps represented by the following formulæ (Ann. **334**, 210):

$$[(CH_2)_3(NR)_3]HI \text{ and } [(CH_2)_3(N_3R_2H)]RI.$$

By the use of aldehydes of higher molecular weight, the tendency to polymerization on the part of the reaction products of primary amines and aldehydes diminishes and "*Schiff's bases*" are formed.

*Methyl*isobutylideneamine*, $(CH_3)_2CH{\cdot}CH{=}N{\cdot}CH_3$, b.p. 68°.



Tetramethylmethylenediamine, $CH_2{<}^{N(CH_3)_2}_{N(CH_3)_2}$, b.p. 85°, is obtained from formaldehyde and dimethylamine (Ber. **26**, R. 934 : Ber. **36**, 1196).

B. Aldoximes, $R'{\cdot}CH{=}N{\cdot}OH$ (V. Meyer, 1863)

The aldoximes are formed when hydroxylamine, in the form of an aqueous solution of hydroxylamine hydrochloride (1 mol.), mixed with an equivalent quantity of sodium hydroxide (½ mol.), acts in the cold on aldehydes. At first there is very evidently formed an unstable addition product, corresponding with aldehyde-ammonia, which in the case of chloral may be obtained in stable form, but which passes readily into the oxime:

$$R{\cdot}CHO + NH_2OH \longrightarrow \underset{\substack{\text{Cannot usually}\\ \text{be isolated.}}}{(R{\cdot}CH(OH){\cdot}NHOH)} \longrightarrow \underset{\text{Aldoxime.}}{R{\cdot}CH:NOH} + H_2O$$

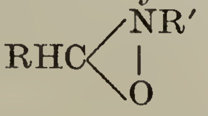
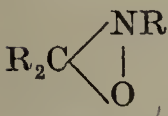
Aldoximes can also be obtained from primary amines by oxidation with permonosulphuric acid, H_2SO_5 (Ber. **35**, 4293), by reduction of αβ-nitroolefines (p. 182) with zinc and acetic acid (C. 1903, II. 553):

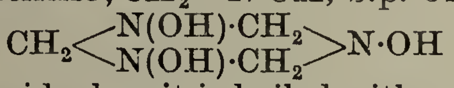
$$CH_3{\cdot}CH_2NH_2 \xrightarrow{O} CH_3CH:NOH$$

$$(CH_3)_2C:CHNO_2 \xrightarrow{H} (CH_3)_2CH{\cdot}CH:NOH$$

The aldoximes are colourless liquids which boil without decomposition. The first members of the series dissolve readily in water. When boiled with acids they are again changed to aldehyde and hydroxylamine. By the action of anhydrides or acid chlorides the aldoximes are converted into nitriles :

$$\underset{\text{Acetoxime.}}{CH_3CH : NOH} + (CH_3CO)_2O = \underset{\text{Acetonitrile.}}{CH_3C \vdots N} + 2CH_3CO_2H.$$

The oximes and hydrazones (p. 252), like the aldehydes, take up hydrocyanic acid ; the products are aminoxyl- or hydrazino-nitriles (Ber. **29**, 62). By the direct action of alkyl halides on aldoximes and ketoximes only alkyl-nitrogen compounds of the iso*oximes* (Vol. II) are formed,  $RHC<\begin{array}{l}NR' \\ | \\ O\end{array}$ and  $R_2C<\begin{array}{l}NR' \\ | \\ O\end{array}$ (C. 1901, I. 1147).

Formaldoxime, $CH_2{=}N{\cdot}OH$, b.p. 84°, passes spontaneously into polymeric *triformoxime*,  $CH_2<\begin{array}{l}N(OH){\cdot}CH_2 \\ N(OH){\cdot}CH_2\end{array}>N{\cdot}OH$ (Ber. **29**, R. 658). Formoxime yields hydrocyanic acid when it is boiled with water (Ber. **28**, R. 233 : C. 1898, II. 18).

Acetaldoxime, $CH_3{\cdot}CH : NOH$, m.p. 47°, b.p. 115°, also exists in a second modification, m.p. 12°, which readily reverts to the first form (Ber. **26**, R. 610 : **27**, 416 : **40**, 1677 : C. 1898, II. 178). Chlorine in hydrochloric acid solution converts it into chloronitrosoethane, $CH_3CHClNO$ (p. 183), which easily becomes rearranged into $CH_3CCl : NOH$.

Chloral hydroxylamine, $CCl_3{\cdot}CH(OH)NH(OH)$, m.p. 98° (Ber. **25**, 702), even upon standing in the air, becomes converted into *Chloraloxime*, $CCl_3CH{=}NOH$, m.p. 39–40°.

Propionaldoxime, $C_2H_5{\cdot}CH{=}N{\cdot}OH$, b.p. 130–132°. iso*Butyraldoxime*, $(CH_3)_2CH{\cdot}CH{=}NOH$, b.p. 139°. iso*Valeraldoxime*, $(CH_3)_2CH{\cdot}CH_2{\cdot}CH{=}NOH$, b.p. 164–165°. *Œnanthaldoxime*, $CH_3(CH_2)_5CH : NOH$, m.p. 55·5°, b.p. 195°. *Myristin aldoxime*, m.p. 82° (Ber. **26**, 2858).

The aldoximes of the fatty series resemble the aromatic *syn*-aldoximes in their behaviour (Ber. **28**, 2019).

C. Diazoparaffins, R·CHN₂

The diazoparaffins, containing the group $:CN_2$, were discovered by Pechmann (1894) to be produced by the action of alkalis on nitrosamines. Diazomethane has been most completely investigated.

The structure of the $:CN_2$ group might be represented either by a ring formula  $\cdot C<\begin{array}{l}N \\ \| \\ N\end{array}$ or an open chain formula $: C : N \vdots N$. In modern formulation this may be represented as containing a semipolar double bond, *i.e.* as $>C \longleftarrow N \vdots N$ or $>C : N \rightrightarrows N$. The physical properties of the compounds (parachor (Ber. **63**, 702) : comparison of b.p. with that of the corresponding halogen and nitro compounds (J.C.S. **1929**, 1108)) are on the whole in better agreement with the ring structure than with a formula containing a co-ordinate linkage, though on account of the existence of optically active diazosuccinic ester (J. Biol. Chem. **55**, 795) which is not compatible with the ring formula, an equilibrium is suggested between the open chain and ring forms (Ber. **63**, 702). Stronger evidence of stereoisomerism at the carbon atom linked to a diazo group has been afforded by a study of the diazo compounds obtained from methyl *cis*.- and *trans*-aminocamphonanates, and the semipolar representation $RR'C \longleftarrow N{\equiv}N$, is suggested for the open chain form (J.A.C.S. **52**, 3004).

Diazomethane, CH_2N_2.—Diazomethane is most readily prepared by the action of alkalis on an ethereal solution of nitrosomethylurethane, potassium methyldiazotate being an intermediate product, which with water yields diazomethane :

$$CH_3{\cdot}N(NO){\cdot}CO_2Et \longrightarrow CH_3{\cdot}N : N{\cdot}OK \longrightarrow CH_2N_2.$$

It is also readily prepared from hydrazine by the action of chloroform and alkalis (Ber. **45**, 501).

$$NH_2{\cdot}NH_2 + CHCl_3 + 3KOH \longrightarrow CH_2N_2 + 3KCl + 3H_2O.$$

Other methods for its preparation are the action of methyldichloroamine on hydroxylamine (Ber. **28**, 1682) and the decomposition of sodium methyl*iso*-diazotate.

It is at ordinary temperature a yellow, odourless, poisonous gas, which attacks the skin, eyes and lungs. It can be condensed to a deep yellow mobile liquid, which boils at − 23° and freezes to a crystalline mass at − 145°. Both as liquid and gas, diazomethane is violently explosive.

It is an extraordinarily reactive compound : its reactions fall into two main groups, (1) where a methyl group is introduced into a compound, with elimination of nitrogen, and (2) the reactions in which the nitrogen forms part of the resulting compound.

Water yields methyl alcohol : acids, organic and inorganic, are converted into their methyl esters, phenols into phenol ethers and aromatic amines into methylated amines (*e.g.* hydrochloric acid yields methyl chloride, phenol, anisole and toluidine, methyltoluidine). Aldehydes are converted by diazomethane into methyl alkyl ketones (Ber. **42**, 2559). Dihydrooxodiazoles (see Vol. II) are probably formed as intermediate compounds. In the case of some aldehydes, particularly those with negative substituents such as chloral and *o*-nitrobenzaldehyde, ethylene oxide derivatives, formed by addition at the C : O linkage, are the main products (Z. angew. Chem. **40**, 1099).

With iodine it forms methylene iodide : when a mixture of CO and diazomethane, diluted with ether, is passed through quartz tubes at 400–500°, small quantities of keten, $CH_2 : CO$, are produced. For dissociation of diazomethane into $(CH_2)_n$ and nitrogen, see Ber. **33**, 956.

Among the reactions in which the nitrogen is retained may be mentioned its addition to acetylene and ethylene, forming respectively pyrazole and pyrazoline (C. 1905, II. 1236), to methyl fumarate yielding the ester of pyrazolinedicarboxylic acid (Ber. **28**, 1624, 2377 : **31**, 2950) and to various cyanogen derivatives forming osotriazole derivatives (Atti. R. Accad. Lincei. [5] **16**, II. **237**, 412 : Gazzetta, 40, I. 120).

For the reaction with quinone, see Ber. **32**, 2292.

Reaction with Grignard Reagents, Monatsh. **34**, 1631.

Diazoethane. See Ber. **31**, 2643.

D. Hydrazones and Azines

By the interaction of an aldehyde and hydrazine, either one or two molecules of aldehyde might react with one molecule of hydrazine, the product in the first case being the hydrazone $R{\cdot}CH : NH{\cdot}NH_2$ and in the second the azine $R{\cdot}CH : NH{\cdot}NH : CH{\cdot}R$. Aliphatic representatives of the aldehyde hydrazones are not known, the azine always being produced.

The products of reaction between the aldehydes and substituted hydrazines, particularly phenylhydrazine, $C_6H_5{\cdot}NH{\cdot}NH_2$ (see Vol. II), and its derivatives are much more important. The phenylhydrazones are obtained by reaction between the aldehyde and phenylhydrazine in alcoholic or acetic acid solution (Fischer, Ann. **190**, 134 : **236**, 137) :

$$R{\cdot}CHO + NH_2{\cdot}NH{\cdot}C_6H_5 \longrightarrow R{\cdot}CH : N{\cdot}NH{\cdot}C_6H_5 + H_2O.$$

Many substitution products of phenylhydrazine such as *p*-nitrophenylhydrazine are much used for the isolation and characterization of aldehydes, as their compounds are less soluble and more easily crystallized.

Aldazines.—*Acetaldazine*, $CH_3{\cdot}CH : N{\cdot}N : C{\cdot}CH_3$, forms a colourless oil readily soluble in water, b.p. 95° (J. pr. Chem. [2], **58**, 325). *Propionaldazine*, b.p. 145°. iso*Butyraldazine*, b.p. 164°.

By adding to acetaldehyde a solution of hydrazine hydrate in a small amount of alcohol, *aldehyde-hydrazine*, $CH_3{\cdot}CH(OH){\cdot}NHNH_2$, H_2O, colourless crystals, m.p. 60°, is formed. This corresponds to aldehyde-ammonia (Ber. **44**, 1134).

From formaldehyde and hydrazine hydrate the two compounds *formalazine*, $CH_2 : N{\cdot}N : CH_2$, an amorphous powder insoluble in water, and the *hydrazone*, $(CH_2 : N{\cdot}NH_2)_2$, a powder soluble in water, are formed under appropriate conditions. The latter gives with silver nitrate an addition compound, $(CH_2 : N{\cdot}NH_2)_3{\cdot}2AgNO_3$. (Ber. **26**, 2360 : **40**, 1505).

Phenylhydrazones.—*Acetaldehyde phenylhydrazone*, $CH_3{\cdot}CH : N{\cdot}NH{\cdot}C_6H_5$, b.p. 140°/20 mm. ; α-form, m.p. 98–101° ; β-form, m.p. 75°, forms a white crystalline mass which is very sensitive towards acids. When recrystallized from 75 per cent. alkaline alcohol the α-modification is obtained ; if it is recrystallized from 75 per cent. alcohol containing SO_2 the labile β-modification is deposited, which gradually changes into the α-form. The two modifications are stereoisomers (p. 41) (Ann. **342**, 15). Structurally isomeric with this compound is benzeneazoethane, $C_6H_5N : N{\cdot}CH_2CH_3$ (Vol. II), which is transformed into acetaldehyde hydrazone by solution in cold concentrated sulphuric acid (Ber. **29**, 793). Aldehyde precipitates a *compound*, $CH_3{\cdot}CHO{\cdot}2(C_6H_5NHNH_2)$, m.p. 77·5°, from the solution of phenylhydrazine bitartrate (Ber. **29**, R. 596).

Propionaldehyde phenylhydrazone, $CH_3{\cdot}CH_2{\cdot}CH{=}N_2C_6H_5$, b.p. 205°/180 mm.

These hydrazones take up hydrocyanic acid and pass into the nitriles of hydrazino-acids (Ber. **25**, 2020).

Formaldehyde differs from the higher homologues in that with phenylhydrazine it yields *trimethylene diphenylhydrazine*, $(C_6H_5N_2)_2(CH_2)_3$, b.p. 183–184° (Ber. **29**, 1473 : R. 777).

2B. OLEFINE ALDEHYDES, $C_nH_{2n-1}{\cdot}CHO$

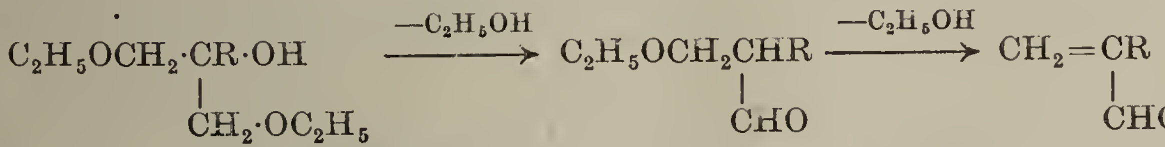
The unsaturated aldehydes, having a double carbon bond, bear the same relation to the olefine alcohols (p. 150) that the saturated aldehydes sustain to their corresponding alcohols. Their aldehyde group shows the same reactive power as the group in the ordinary aldehydes, but the presence of the unsaturated residue, C_nH_{2n-1}, gives rise to addition-reactions similar to those shown by the olefines.

$\alpha\beta$-Olefine aldehydes result from the following special methods :

(1) By the condensation of aldehydes of the formula $RCH_2{\cdot}CHO$ by zinc chloride, hydrochloric acid, etc., during which water is split off from the aldol first formed.

$$\underset{\text{Acetaldehyde.}}{2CH_3CHO} \longrightarrow \underset{\text{Aldol.}}{CH_3CHOH{\cdot}CH_2CHO} \longrightarrow \underset{\text{Crotonaldehyde.}}{CH_3CH : CHCHO}$$

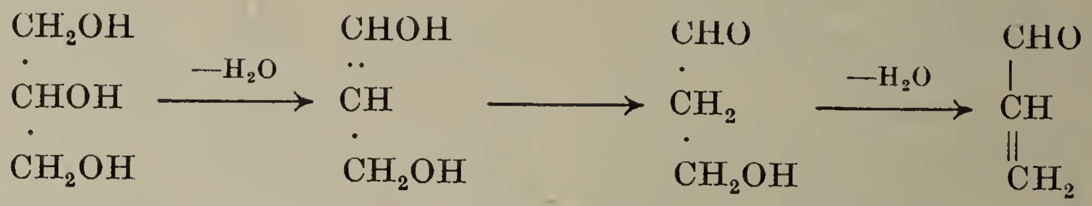
(2) From glycerol and from the dialkyl ethers of homologous glycerols, by heating with anhydrous oxalic acid, accompanied by the expulsion of water or alcohol, similarly to the formation of paraffin aldehydes from ethylene glycol ethers (p. 227 ; Ann. Chim. Phys. [8] 9, 560) :



$$\underset{\displaystyle CH_2{\cdot}OC_2H_5}{C_2H_5OCH_2{\cdot}\overset{}{CR}{\cdot}OH} \xrightarrow{-C_2H_5OH} \underset{\displaystyle CHO}{C_2H_5OCH_2CHR} \xrightarrow{-C_2H_5OH} \underset{\displaystyle CHO}{CH_2{=}CR}$$

Acrolein (*Acraldehyde*), $CH_2 : CH{\cdot}CHO$ (see Ann. Chim. [9] **15**, 160 *et seqq.*). Acrolein is prepared by the distillation of glycerol with potassium bisulphate (Ber. **20**, 3388 : Ann. Suppl. 3, 180 : C. 1900, I. 962 : Ber. **35**, 1137 : Compt. rend. **151**, 530), boric acid (Ber. **32**, 1352), phosphoric acid (J. pr. Chem. [2] 79, 351), magnesium sulphate

(Ber. **45**, 2046), and other dehydrating agents, and by passing anhydrous glycerol over heated alumina. It is also formed when fats are distilled.



$$\begin{array}{c} CH_2OH \\ \cdot \\ CHOH \\ \cdot \\ CH_2OH \end{array} \xrightarrow{-H_2O} \begin{array}{c} CHOH \\ \cdot\cdot \\ CH \\ \cdot \\ CH_2OH \end{array} \longrightarrow \begin{array}{c} CHO \\ \cdot \\ CH_2 \\ \cdot \\ CH_2OH \end{array} \xrightarrow{-H_2O} \begin{array}{c} CHO \\ | \\ CH \\ \| \\ CH_2 \end{array}$$

Acrolein is a colourless mobile liquid, b.p. 52°, m.p. – 87°, D_{20} 0·8410. It has an intolerable suffocating odour. It rapidly polymerizes to *disacryl*. It is soluble in 2–3 parts of water and reduces an ammoniacal silver solution with formation of a silver mirror. It oxidizes in the air to acrylic acid. Nascent hydrogen reduces it to allyl alcohol: it can, however, be reduced catalytically in the presence of nickel to propionic aldehyde and propyl alcohol (Ann. Chim. Phys. [8] **4**, 399: Ann. Chim. [9] **15**, 203).

It reacts with sodium bisulphite with the formation of the compound $NaSO_3\cdot CH_2\cdot CH_2\cdot CH(OH)\cdot SO_3Na$ from which the aldehyde cannot be regenerated (Ber. **6**, 1445: Ann. **233**, 36). When heated for a long time with alcohol, it forms β-ethoxypropionaldehyde acetal, $EtO\cdot CH_2\cdot CH_2\cdot CH(OEt)_2$ (Ber. **31**, 1014). Both these reactions demonstrate the heightened reactivity of the ethylene linkage in the proximity of the : CO group.

Phosphorus pentachloride converts acrolein into *dichloropropylene*, $CH_2:CH\cdot CHCl_2$, b.p. 84°. With hydrochloric acid it yields *β-chloropropionaldehyde* (p. 240). With bromine it yields a *dibromide*, $CH_2\cdot Br\cdot CHBr\cdot CHO$, which becomes converted into glyceric aldehyde when heated with water, and into αβ-dibromopropionic acid upon oxidation with nitric acid. Barium hydroxide solution converts it into *α-acrose* or dl-*fructose* (*q.v.*) (Ber. **20**, 3388).

When kept for some length of time, acrolein passes into an amorphous, white mass (*disacryl*). On warming the HCl compound of acrolein (see above) with alkalis or potassium carbonate *metacrolein*, m.p. 45°, is obtained. The vapour density of this agrees with the formula $(C_3H_4O)_3$.

Ammonia changes acrolein into *acrolein-ammonia*, $2C_3H_4O + NH_3 = C_6H_9NO + H_2O$. This is a yellowish mass which on drying becomes brown, and forms amorphous salts with acids. It yields *picoline*, $C_5H_4N\cdot CH_3$ (*q.v.*), when distilled. Hydrazine changes acrolein to pyrazoline, and phenylhydrazine converts it into 1-phenylpyrazoline (Ber. **28**, R. 69).

Acrolein acetal, $CH_2:CH\cdot CH(OC_2H_5)_2$, b.p. 123°, is formed by the action of powdered potassium hydroxide on chloropropionaldehyde acetal, which is prepared from acrolein by means of alcohol and hydrochloric acid (Ber. **31**, 1797) (see also glyceraldehyde).

Crotonaldehyde, $CH_3\cdot CH:CH\cdot CHO$, b.p. 104°, D = 1·033 (*Kekulé*, Ann. **162**, 91), is obtained from aldol, formed by the condensation of acetaldehyde (p. 390) by heating it with dilute hydrochloric acid, with water and zinc chloride, or with a sodium acetate solution, to 100° (Ber. **14**, 514: **25**, R. 732). It is most readily prepared by introducing paraldehyde into cooled concentrated sulphuric acid (Compt. rend. **147**, 1316).

Crotonaldehyde is a liquid with an irritating odour; it becomes oxidized by the air to crotonic acid, and it reduces silver oxide (Ber. **29**, R. 290). It combines with hydrochloric acid to form *β-chlorobutyraldehyde* (p. 240); on standing with hydrochloric acid it unites with water and re-forms aldol. Iron and acetic acid reduce it to crotonyl alcohol, butyraldehyde and butyl alcohol. It can be hydrogenated catalytically in the presence of platinum, copper or nickel with the formation of butyraldehyde and butyl alcohol (Bull. Soc. Chim. [4], **7**, 23: **9**, 922: Brit. Chem. Abst. 1926, B. 108).

When the alcoholic solution of acetaldehyde-ammonia is heated to 120°, *crotonal-ammonia*, *oxytetraldine*, $C_8H_{13}NO$, is produced. It is a brown, amorphous mass. When heated it breaks up into water and *collidine*, $C_5H_2N(CH_3)_3$, a pyridine derivative (Vol. II).

Tiglic aldehyde, *Guaiol,* $CH_3CH{=}C(CH_3)\cdot CHO$, b.p. 116°, may be obtained by the distillation of guaiacol resin, and by the condensation of acetaldehyde and propaldehyde.

Δα-α-Methylpentenaldehyde, methylethylacrolein, $C_2H_5\cdot CH : C(CH_3)\cdot CHO$, b.p. 137°, is produced by the condensation of propionaldehyde (p. 238).

α-Propylacrolein, b.p. 117°, iso*butylacrolein,* b.p. 133°, and *amylacrolein,* b.p. 59°/13 mm., $CH_2 : CR\cdot CHO$, are prepared from the respective glycerol ethers (method of formation 2, p. 253).

Δα-Hexenaldehyde, $CH_3(CH_2)_2CH : CH\cdot CHO$, b.p. 47°/17 mm., is a characteristic component of the oil derived from green leaves (Ann. **390,** 89 : **404,** 93).

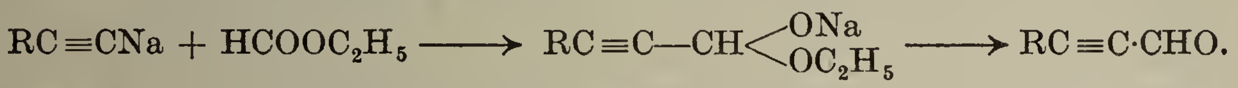
Citronellal and its isomer *rhodinal* are olefine aldehydes and *geranial* or *citral* belongs to the class of diolefine aldehydes. These will be considered under the olefine terpenes (Vol. II).

2C. ACETYLENE ALDEHYDES, $C_nH_{2n-3}\cdot CHO$

Propiolaldehyde.—*Propargylic aldehyde,* $CH \vdots C\cdot CHO$, b.p. 59°, is produced when the *acetal,* $CH \vdots C\cdot CH(OC_2H_5)_2$, b.p. 140°, formed from dibromacrolein acetal and alcoholic potassium hydroxide, is boiled with dilute sulphuric acid. It is a very mobile liquid, which provokes tears. Its *silver salt* is very explosive. Sodium hydroxide at the ordinary temperature decomposes propargylic aldehyde instantly into acetylene and sodium formate : $CH \vdots C\cdot CHO + NaOH = CH \vdots CH + NaO\cdot CHO$ (*Claisen,* Ber. **31,** 1021).

Tetrolaldehyde, *methylpropiolaldehyde,* $CH_3\cdot CH \vdots CH\cdot CHO$, b.p. 107°, is obtained from crotonaldehyde dibromide by a similar reaction. Alkalis decompose it into allylene and allyl formate. *Oxime,* m.p. 103° : *hydrazone,* b.p. 64° (Ber. **44,** 1162 : Ann. Chim. Phys. [8] **28,** 433).

Homologous acetylenic aldehydes or their acetals are obtained from the sodium derivatives or magnesium halide derivatives of acetylene by their reaction with formic or orthoformic esters (C. 1904, II. 187).

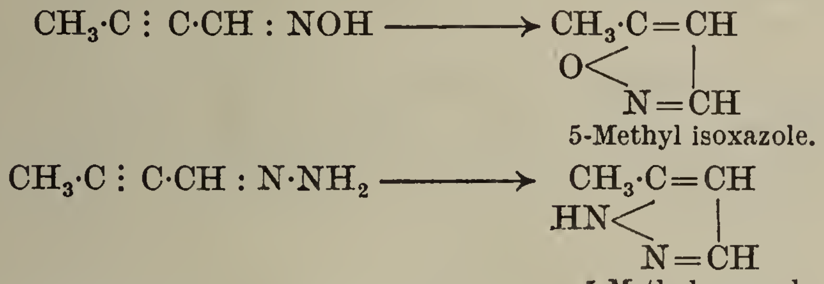


$$RC{\equiv}CNa + HCOOC_2H_5 \longrightarrow RC{\equiv}C{-}CH{<}^{ONa}_{OC_2H_5} \longrightarrow RC{\equiv}C\cdot CHO.$$

$$RC{\equiv}CMgI + HC(OC_2H_5)_3 \longrightarrow RC{\equiv}C\cdot CH(OC_2H_5)_2 \longrightarrow RC{\equiv}C\cdot CHO.$$

Amylpropiolic aldehyde, $C_5H_{11}C{\equiv}C\cdot CHO$, b.p. 89°/26 mm., *acetal,* b.p. 110°/11 mm. and **hexylpropriolic aldehyde,** $C_6H_{13}C{\equiv}C\cdot CHO$, b.p. 91°/13 mm., *acetal,* b.p. 127°/12 mm., are prepared in this way from œnanthylidene and caprylidene, respectively.

The *oximes* and *hydrazones* of these acetylenic aldehydes are very easily isomerized, particularly by alkaline reagents, to isoxazole and pyrazole derivatives.



5-Methyl isoxazole.

5-Methyl pyrazole.

The propargylaldehyde derivatives are so easily isomerized that the oxime and hydrazone cannot be isolated (Ber. **36,** 3665 : C. 1904, II. 187).

3A. SATURATED KETONES, $C_nH_{2n}O$

The great similarity between the aldehydes and ketones finds expression in their most important methods of formation and in their reactions. Two different kinds of ketones are known :

1. Simple ketones, containing two similar alkyl groups.
2. Mixed ketones, having two different alkyl groups.

Methods of Formation

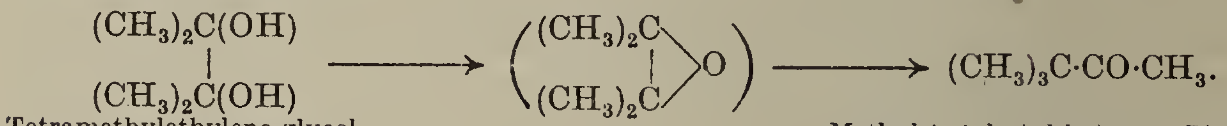
(1) Oxidation of secondary alcohols, whereby the $=CH\cdot OH$-group is converted into the $=CO$-group (p. 224).

(2) By hydrolysis of such derivatives as oximes, hydrazones, semicarbazones, *gem*-dihalogen compounds, etc., just as aldehydes are obtained from their corresponding derivatives.

(3) By the isomerization of di-tertiary and secondary-tertiary $\alpha\beta$-glycols under the influence of hydrochloric or sulphuric acid, with loss of water, exactly as glycols containing a primary alcohol group are changed into aldehydes.

$$R_2C(OH)\cdot CHR'\cdot OH \longrightarrow R_2CH\cdot CO\cdot R' + H_2O.$$

The change of di-tertiary glycols, known as *pinacols* or *pinacones*, into ketones or *pinacolins* is accompanied by the migration of an alkyl group. The simplest of the di-tertiary glycols is tetramethylethylene glycol, or *pinacone*, from which the abstraction of water should produce tetramethylethylene oxide. Instead, this substance becomes rearranged internally to form the simplest *pinacolin*, methyl *tert.*-butyl ketone :



$$\begin{array}{c}(CH_3)_2C(OH)\\ |\\ (CH_3)_2C(OH)\end{array} \longrightarrow \left(\begin{array}{l}(CH_3)_2C\\ \quad\;\; |\\ (CH_3)_2C\end{array}\!\!>O\right) \longrightarrow (CH_3)_3C\cdot CO\cdot CH_3.$$

Tetramethylethylene glycol.
Pinacone.

Methyl *tert.*-butyl ketone : Pinacolin.

Definite intermediate products such as ethylene oxides cannot be isolated in the pinacolin transformation, so that the reaction would appear to be a true intramolecular migration (Ann. **396,** 200). (Discussion of mechanism of pinacol-pinacolin rearrangement, with literature, see Annual Reports, 1930, **27,** 114.)

(4) From the sodium salts of the secondary nitroparaffins by treatment with acids (Ann. **280,** 267). (Compare method 8 for the preparation of aldehydes.)

$$2(CH_3)_2C : NOONa + 2HCl \longrightarrow 2(CH_3)_2CO + N_2O + 2NaCl + H_2O.$$

The secondary nitroparaffins can also be converted into ketones by reducing them with stannous chloride and strong hydrochloric acid, whereby ketoximes are produced and can be hydrolysed to the ketone (C. 1899, I. 597), or by oxidation in alkaline solution with potassium permanganate (C. 1914, I. 757).

(5) By hydrolysis of the ethers of $\alpha\beta$-olefine alcohols (p. 158); (C. 1904, I. 719) :

$$C_5H_{11}C(OCH_3) : CH_2 \xrightarrow[H_2SO_4]{\text{dilute}} C_5H_{11}\cdot COCH_3 + CH_3OH.$$

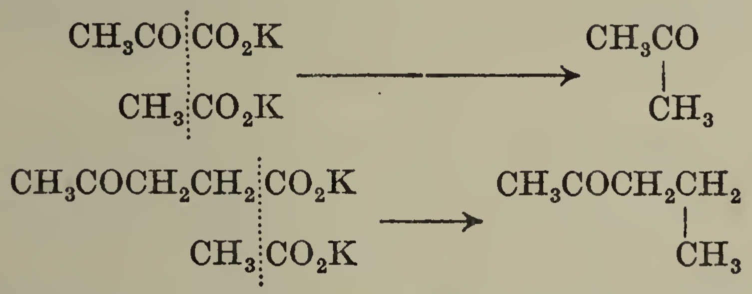
Nucleus-synthetic Methods of Formation.—(6) By the distillation of calcium or barium acetates and their higher homologues. Such a salt, when heated alone, yields a simple ketone, but a mixture of equimolecular quantities of the salts of two acids results in the formation of mixed ketones (p. 225).

In the formation of ketones with high molecular weight it is best to carry out the distillation under diminished pressure. Some normal fatty acids yield ketones on treatment with P_2O_5 (Ber. **26,** R. 495).

It has been recommended to distil the acids with calcium carbide (Ber. **39,** 1703).

The very smooth formation of ketones by leading the vapours of fatty acids over heated alumina, manganous oxide, calcium carbonate, etc., depends on a similar breakdown of the momentarily-formed fatty acid salts (Ann. Chim. Phys. [8] **28,** 243 : Compt. rend. **156,** 1730 : **158,** 830). Ketones of high molecular weight are also formed by distilling the higher fatty acids with iron filings (J.C.S. **99,** 2298).

(7) By the electrolysis of a mixture of the potassium salts of a keto-carboxylic and a fatty acid :

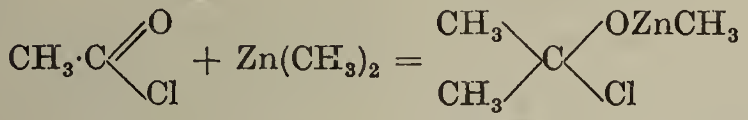


$$\begin{matrix} CH_3CO \vdots CO_2K \\ CH_3 \vdots CO_2K \end{matrix} \longrightarrow \begin{matrix} CH_3CO \\ | \\ CH_3 \end{matrix}$$

$$\begin{matrix} CH_3COCH_2CH_2 \vdots CO_2K \\ CH_3 \vdots CO_2K \end{matrix} \longrightarrow \begin{matrix} CH_3COCH_2CH_2 \\ | \\ CH_3 \end{matrix}$$

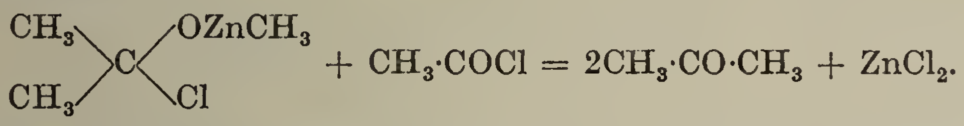
(8) By the action of the zinc alkyls on the acid chlorides (*Freund,* 1860).

The reaction is similar to that occurring in the formation of the tertiary alcohols (p. 132). At first the same intermediate product is produced (Ann. **175,** 361 ; **188,** 104) :



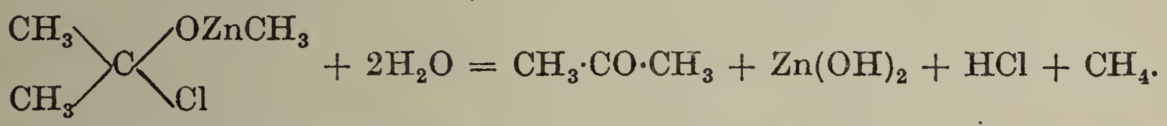
$$CH_3{\cdot}C{\begin{matrix} {/\!\!/}O \\ \diagdown Cl \end{matrix}} + Zn(CH_3)_2 = \begin{matrix} CH_3 \\ CH_3 \end{matrix}{>}C{<}\begin{matrix} OZnCH_3 \\ Cl \end{matrix}$$

which (with a second molecule of the acid chloride) afterwards yields the ketone and zinc chloride :



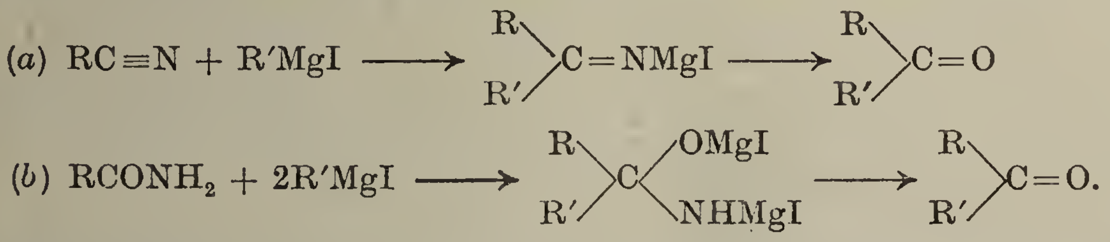
$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}{>}C{<}\begin{matrix} OZnCH_3 \\ Cl \end{matrix} + CH_3{\cdot}COCl = 2CH_3{\cdot}CO{\cdot}CH_3 + ZnCl_2.$$

In many cases, especially in the preparation of the ordinary pinacolin from trimethylacetyl chloride and zinc methyl, it is preferable to decompose immediately the addition product of zinc methyl and acid chloride with water, when the zinc hydroxide will be converted by the hydrochloric acid into zinc chloride :



$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}{>}C{<}\begin{matrix} OZnCH_3 \\ Cl \end{matrix} + 2H_2O = CH_3{\cdot}CO{\cdot}CH_3 + Zn(OH)_2 + HCl + CH_4.$$

(9) By the action of alkyl magnesium halides, ketones as well as aldehydes (mode of formation 10, p. 228) can be prepared, (*a*) from nitriles, and (*b*) from acid amides (C. 1902, I. 299 : 1903, II. 1110).



$$(a)\ RC{\equiv}N + R'MgI \longrightarrow \begin{matrix} R \\ R' \end{matrix}{>}C{=}NMgI \longrightarrow \begin{matrix} R \\ R' \end{matrix}{>}C{=}O$$

$$(b)\ RCONH_2 + 2R'MgI \longrightarrow \begin{matrix} R \\ R' \end{matrix}{>}C{<}\begin{matrix} OMgI \\ NHMgI \end{matrix} \longrightarrow \begin{matrix} R \\ R' \end{matrix}{>}C{=}O.$$

Ketones are also obtained by the action of the magnesium alkyl halides on acid anhydrides (Bull. Soc. Chim. [4] **7,** 836) and sodium salts of the fatty acids (Ber. **42,** 4500).

(10) By the action of diazomethane (p. 251), the aldehydes can be converted into alkyl methyl ketones (Ber. **40,** 481) :

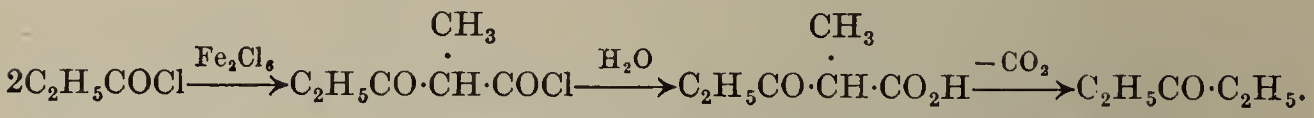
$$C_6H_{13}COH + CH_2N_2 = C_6H_{13}CO{\cdot}CH_2 + N_2.$$

Ethylene oxides are sometimes formed in this reaction. See p. 228.

(11) By heating ketones with alkyl iodides and potassium hydroxide at 100–140°, or better, by the action of sodamide and alkyl iodides in presence of ether, the hydrogen atoms attached to the carbon atoms adjacent to the CO group can be replaced by alkyl groups (Ann. Chim. Phys. [8] **28,** 732 : **29,** 313 : Ann. **310,** 323), *e.g.* :

$$CH_3\cdot CH_2\cdot CO\cdot CH_2\cdot CH_3 \longrightarrow CHMe_2\cdot CO\cdot CHMe_2 \longrightarrow CMe_3\cdot CO\cdot CMe_3.$$

(12) By the action of anhydrous ferric chloride on the acid chlorides. Hydrochloric acid is set free, and chlorides of β-ketone-carboxylic acids are produced. From these water liberates the free β-ketone-carboxylic acids which readily break down into carbon dioxide and ketones :



$$2C_2H_5COCl \xrightarrow{Fe_2Cl_6} C_2H_5CO\cdot\overset{CH_3}{\dot{C}H}\cdot COCl \xrightarrow{H_2O} C_2H_5CO\cdot\overset{CH_3}{\dot{C}H}\cdot CO_2H \xrightarrow{-CO_2} C_2H_5CO\cdot C_2H_5.$$

(13) By the oxidation of dialkylacetic acids, and the α-hydroxy-dialkylacetic acids corresponding with them ; the latter are formed as intermediate products in the oxidation of the former compounds, *e.g.* :

$$(CH_3)_2CH\cdot CO_2H \xrightarrow{O} (CH_3)_2C(OH)\cdot CO_2H \xrightarrow{O} (CH_3)_2CO + CO_2 + H_2O.$$

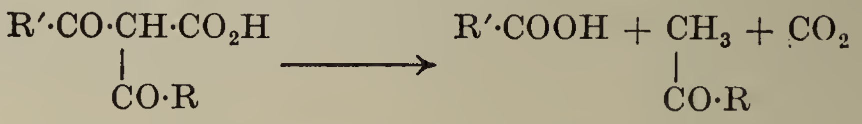
(14) Ketones are formed by the hydrolysis of β-ketocarboxylic acids by dilute acids (for details, see under acetoacetic ester) :

$$CH_3\cdot CO\cdot CRR'\cdot CO_2H \longrightarrow CH_3\cdot CO\cdot CHRR' + CO_2.$$

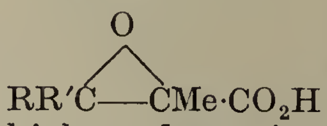
Acetonedicarboxylic acid and its derivatives break down similarly (*cf.* Ber. **42,** 3176 : Ann. **398,** 242) :

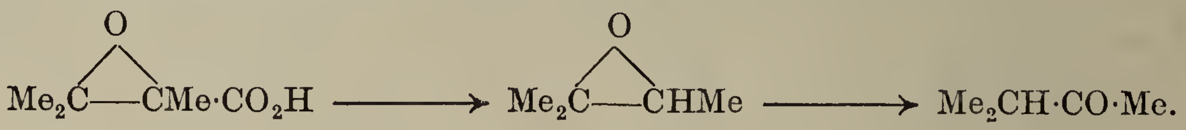
$$HOCO\cdot CH_2\cdot CO\cdot CH_2\cdot CO_2H \longrightarrow CH_3\cdot CO\cdot CH_3 + 2CO_2.$$

Finally, diacylacetic acids break down with formation of a carboxylic acid, ketone and CO_2 (C. 1903, I. 225) :



$$\underset{\displaystyle CO\cdot R}{R'\cdot CO\cdot CH\cdot CO_2H} \longrightarrow R'\cdot COOH + \underset{\displaystyle CO\cdot R}{CH_3} + CO_2$$

(15) The glycidic acids of the general type  readily break down into CO_2 and alkylene oxides, which undergo isomerization to the ketone (Compt. rend. **141,** 766), *e.g.* :



Ketones are produced in the dry distillation of citric acid, sugar, cellulose (wood), and of many other carbon compounds, so that they are found in coal and coal-tar (Ber. **36,** 254, 2713).

Nomenclature and Isomerism.—The term ketone is derived from the simplest and first-discovered ketone—acetone. The names of the ketones are obtained by associating the names of the alkyls with the word ketone—*e.g.* dimethyl ketone, methylethyl ketone, etc.

The " Geneva names " are obtained by adding the suffix " one " to the name of the hydrocarbon : acetone is called [Propanone], and methylethyl ketone is [Butanone].

As there is a ketone for every secondary alcohol, the number of isomeric ketones of definite carbon content is equal to the number of possible secondary alcohols containing the same number of carbon atoms. The simple ketones are isomeric with the mixed ketones having a like carbon content. The isomerism of the ketones among themselves is dependent upon the homology of the alcohol radicals united with the CO-group. The saturated ketones are isomeric with the saturated aldehydes, the olefinic alcohols and the ethylene oxides.

Properties and Reactions.

The ketones are neutral bodies. The lower members of the series are volatile, ethereal-smelling liquids, whilst the higher members are solids.

(1) Ketones differ chiefly from aldehydes in their behaviour when oxidized. They are not capable of reducing an alkaline silver solution, and are not so easily oxidized as the aldehydes.

When the more powerful oxidants are employed, the ketones almost invariably break down at the union with the CO-group: carboxylic acids are produced, and in some cases ketones with a lower carbon content:

$$\begin{array}{l} CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow CH_3{\cdot}CO_2H \text{ and } H{\cdot}CO_2H \xrightarrow{O} CO_2 + H_2O \\ C_2H_5{\cdot}CO{\cdot}C_2H_5 \longrightarrow C_2H_5{\cdot}CO_2H \text{ and } CH_3{\cdot}CO_2H. \end{array}$$

In the case of mixed ketones, when both alcohol radicals are primary in character, the CO-group does not remain exclusively with the lower alcohol radical, but the reaction proceeds in both possible directions, *e.g.*:

$$CH_3CH_2{\cdot}CO{\cdot}CH_2CH_2CH_3 - \left\langle \begin{array}{l} \nearrow CH_3{\cdot}CO_2H \text{ and } CO_2H{\cdot}CH_2CH_2CH_3 \\ \searrow 2CH_3CH_2{\cdot}CO_2H \end{array} \right.$$

When a secondary alcohol radical is present it splits off as ketone, and is then further oxidized, whilst with a tertiary alcohol radical the CO-group remains combined as carboxyl.

The direction in which the oxidation proceeds is dependent less upon the oxidizing agent than upon the oxidation temperature (Ann. **161**, 285: **186**, 257: Ber. **15**, 1194: **17**, R. 315: **18**, 2266, R. 178: **25**, R. 121).

It is remarkable that pinacolin (p. 265) is successfully oxidized by potassium permanganate to the corresponding α-ketone-carboxylic acid with the same number of carbon atoms: trimethylpyruvic acid:

$$\underset{\text{Pinacolin.}}{(CH_3)_3C{\cdot}CO{\cdot}CH_3} \xrightarrow{3O} \underset{\text{Trimethylpyruvic acid.}}{(CH_3)_3C{\cdot}CO{\cdot}CO_2H.}$$

Hydrogen peroxide changes acetone into a peroxide (p. 265) which breaks up into acetol, CH_3COCH_2OH, and pyruvic acid, $CH_3CO{\cdot}COOH$ (C. 1905, II. 212).

(2) Concentrated nitric acid converts the ketones in part into dinitroparaffins (p. 185):

$$\begin{array}{r} (C_2H_5)_2CO \xrightarrow{HNO_3} CH_3CH(NO_2)_2 \\ (CH_3CH_2CH_2)_2CO \longrightarrow CH_3{\cdot}CH_2CH(NO_2)_2 \end{array}$$

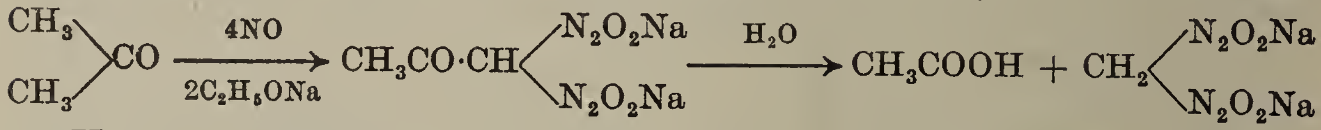
α-Diketones may be formed at the same time if the ketone be suitably constituted, *e.g.* *iso*propyl *iso*butyl ketone (C. 1900, II. 124).

(3) Amyl nitrite, in the presence of sodium ethoxide or hydrochloric acid, converts the ketones into *iso*nitroso-ketones:

$$\begin{array}{r} CH_3{\cdot}CO{\cdot}CH_3 \xrightarrow{C_5H_{11}NO_2} CH_3{\cdot}CO{\cdot}CH(NOH) \\ CH_3CO{\cdot}CH_2{\cdot}CH_3 \longrightarrow CH_3{\cdot}CO{\cdot}C(NOH){\cdot}CH_3. \end{array}$$

The *iso*nitroso-ketones will be considered later as monoximes of α-keto-aldehydes, or α-diketones.

(4) Ketones, containing the carbonyl group next to a methyl or methylene group, are acted on by nitric oxide in presence of sodium ethoxide, and form the sodium salt of di-*iso*nitramino-ketones. These are decomposed by water into a carboxylic acid and the sodium salt of a di-*iso*nitraminoolefine (p. 184; Ann. **300**, 95):



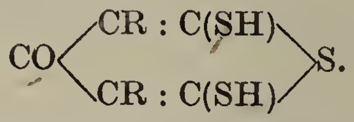
$$(CH_3)_2CO \xrightarrow[2C_2H_5ONa]{4NO} CH_3CO{\cdot}CH(N_2O_2Na)_2 \xrightarrow{H_2O} CH_3COOH + CH_2(N_2O_2Na)_2$$

Ketones containing the group $CH_3{\cdot}CO{\cdot}$ yield iodoform (p. 291) when treated with iodine and an alkali hydroxide.

(5) The hexaalkylacetones are decomposed when heated with sodamide in benzene solution with sodamide into trialkylacetamides and trialkylmethanes (Compt. rend. **150**, 661):

$$Me_3C{\cdot}CO{\cdot}CMe_3 \longrightarrow Me_3{\cdot}CONH_2 + CHMe_3.$$

(6) By the action of carbon bisulphide and alkali hydroxides on ketones of the type $R{\cdot}CH_2{\cdot}CO{\cdot}CH_2R$, orange-red coloured acids, probably of the following general formula, are produced (Ber. **38**, 2888):



$$CO\left\langle\begin{matrix}CR : C(SH)\\CR : C(SH)\end{matrix}\right\rangle S.$$

A large number of the addition reactions shown by ketones are due, as in the case of the aldehydes, to addition at the C : O double bond. The first-formed addition product frequently loses water with formation of an unsaturated compound.

(7) *Reduction.*—By the action of nascent hydrogen (from sodium amalgam or electrolytic hydrogen (C. 1900, II. 795)) or catalytically in the presence of platinum or nickel (C. 1912, I., 1273: 1914, I., 1993) ketones are reduced to the secondary alcohol from which they are produced by oxidation. Ditertiary glycols, the so-called pinacones, are simultaneously produced:

$$R{\cdot}CO{\cdot}R' + 2H \longrightarrow R{\cdot}CH(OH){\cdot}R'$$

$$2R{\cdot}CO{\cdot}R' + 2H \longrightarrow \begin{matrix}R{\cdot}C(OH){\cdot}R'\\ |\\ R{\cdot}C(OH){\cdot}R'.\end{matrix}$$

(8) The CO group in mixed aliphatic-aromatic and wholly aromatic ketones can be reduced to CH_2 by boiling with amalgamated zinc and concentrated hydrochloric acid (*Clemmensen*, Ber. **46**, 1837). Paraffins can be obtained from ketones by heating their hydrazones with sodium ethylate, nitrogen being expelled (Ann. **394**, 86).

(9) The ketone derivatives $R_2C(OR')_2$, corresponding with the acetals (p. 266), are produced when the β-dialkoxycarboxylic acids, $RC(OC_2H_5)_2CH_2CO_2H$, lose CO_2. They are prepared by the interaction of ketones and orthoformic ester; or in general from imidoether hydrochlorides and alcohols (*Claisen*, Ber. **31**, 1010: Ber. **40**, 3021).

(10) The ketones resemble the aldehydes in their behaviour with hydrogen sulphide and mercaptans in presence of hydrochloric acid.

The products are the polymeric thioketones (p. 266) and the mercaptoles, $RR'C(SR'')_2$ (p. 267).

(11) Only such ketones as contain a methyl group form addition compounds with sodium bisulphite, and on the analogy of the aldehyde bisulphites (p. 266) these compounds are to be regarded as the sodium salts of hydroxysulphonic acids:

$$R{\cdot}COMe + NaHSO_3 \longrightarrow RMeC(OH){\cdot}SO_3Na.$$

(12) Ammonia reacts with ketones differently from its reaction with aldehydes. The "ketone-ammonias" are not formed, but condensation products from more than one molecule of ketone are produced. Thus, from acetone and ammonia, diacetoneamine, and triacetoneamine are produced. These are discussed fully on p. 274 (see Ber. **42,** 3298).

(13) Ketones react with hydroxylamine, hydrazine, phenylhydrazine and semicarbazide with the formation of oximes (p. 267), hydrazones and azines (p. 268) phenylhydrazones (p. 269) and semicarbazones (p. 269).

(14) Phosphorus pentachloride, phosphorus trichloro-dibromide, and phosphorus pentabromide replace the oxygen of the ketones by two chlorine or two bromine atoms.

This reaction can be employed for the preparation of dichloro- or dibromoparaffins in which an intermediate C-atom carries the two halogen atoms. As these ketone chlorides readily exchange their chlorine for hydrogen, they constitute a means of converting the ketones into the corresponding paraffins (p. 95).

Halogenolefines formed by the loss of halogen acid accompany the dihalogenparaffins. Halogen-ketones are also formed by direct substitution (C. 1913, I. 1004).

(15) The hydrogen atoms of the alkyl groups present in the ketones can be replaced by chlorine and bromine.

(16) Boiling with acid chlorides, especially benzoyl chloride, converts many ketones into esters of the tautomeric $\alpha\beta$-olefine alcohols (p. 150), $RC(O{\cdot}COC_6H_5):CHR'$.

(17) Paraffin ketones, unlike the lower members of the aldehyde series, do not form polymeric modifications.

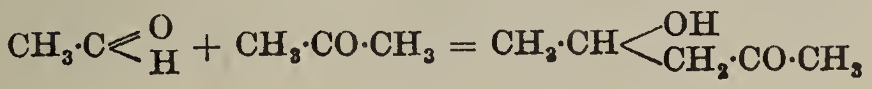
Nuclear Synthetic Reactions.

The action of ammonia on acetone and the formation of pinacones by reduction of ketones which have already been mentioned are examples of this type of reaction. The following reactions are more important.

(18) Just as two aldehyde molecules can condense to aldols, so two molecules of acetone condense in the presence of cold concentrated sodium hydroxide to diacetonealcohol (*q.v.*):

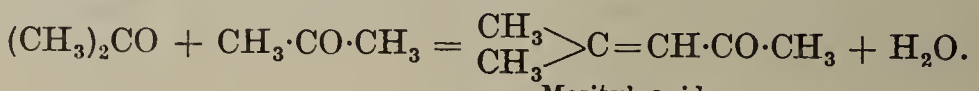
$$2CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow (CH_3)_2C(OH){\cdot}CH_2{\cdot}CO{\cdot}CH_3.$$

Similarly aldehyde or chloral will unite with acetone, forming hydracetylacetone and trichlorohydracetylacetone (*q.v.*):



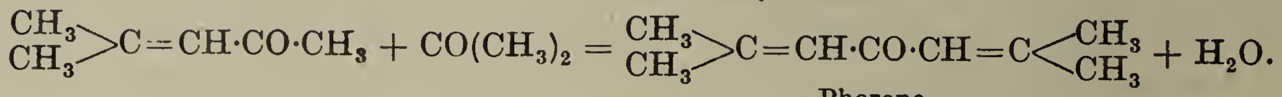
$$CH_3{\cdot}C\Big<\begin{matrix}O\\H\end{matrix} + CH_3{\cdot}CO{\cdot}CH_3 = CH_3{\cdot}CH\Big<\begin{matrix}OH\\CH_2{\cdot}CO{\cdot}CH_3\end{matrix}$$

Acetone also condenses with other aldehydes,—*e.g.* benzaldehyde. But it is impossible to obtain the ketone-alcohols which form at first. There is a loss of water, and unsaturated derivatives are produced, just as in the condensation of two molecules of aldehyde to form crotonaldehyde. Thus, two molecules of acetone, in the presence of $ZnCl_2$, HCl, or H_2SO_4, unite directly, with the elimination of water, to form *mesityl oxide* (p. 273), which in turn condenses with a third molecule of acetone to form *phorone* (p. 273).



$$(CH_3)_2CO + CH_3{\cdot}CO{\cdot}CH_3 = {CH_3 \atop CH_3}{>}C{=}CH{\cdot}CO{\cdot}CH_3 + H_2O.$$

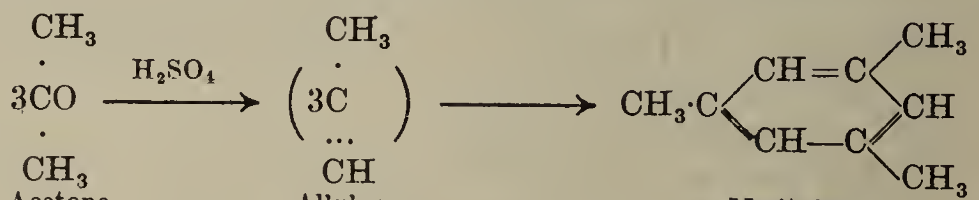
Mesityl oxide.



$${CH_3 \atop CH_3}{>}C{=}CH{\cdot}CO{\cdot}CH_3 + CO(CH_3)_2 = {CH_3 \atop CH_3}{>}C{=}CH{\cdot}CO{\cdot}CH{=}C{<}{CH_3 \atop CH_3} + H_2O.$$

Phorone.

(19) Acetone and other ketones, having a suitable constitution, change into symmetrical trialkylbenzenes, under the influence of concentrated sulphuric acid, probably with intermediate formation of alkyl acetylenes (p. 111). Acetone yields mesitylene:



Acetone. Allylene. Mesitylene.

(20) Acetone condenses, in presence of lime or sodium ethylate, to iso*phorone*, a trimethyl*cyclo*hexenone (*q.v.*). Higher condensation products, the so-called xylitones, are also formed.

(21) With the alkyl magnesium halides ketones form addition products which form tertiary alcohols when decomposed with water (see p. 133). Ketones do not, in general, react with the zinc alkyls, but tertiary alcohols are obtained by the simultaneous action of zinc and alkyl iodides on ketones.

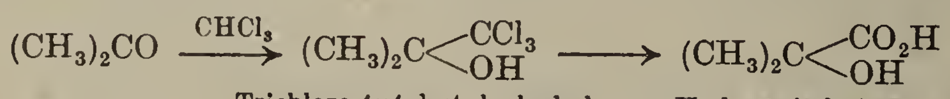
(22) Ketones combine with chloroacetic ester and α-chloropropionic ester in the presence of sodium ethoxide or sodamide to form glycidic esters (C. 1905, I. 346: 1906, I. 22: Ber. **38**, 699).

(23) Ketones also unite with hydrogen cyanide to form "cyanohydrins," which will be described later as the nitriles of α-hydroxy acids. The cyanohydrins are converted into the hydroxy acids by hydrolysis with hydrochloric acid:

$$R_2CO + HCN \longrightarrow R_2C(OH){\cdot}CN \longrightarrow R_2C(OH){\cdot}CO_2H.$$

The ketones also combine with ammonium cyanide to form α-amino acid nitriles: these can also be obtained from the cyanohydrins by the action of ammonia.

(24) Acetone, in the presence of sodium hydroxide, combines with chloroform, yielding trichloro-*tert.*-butyl alcohol, which is a derivative of α-hydroxy*iso*butyric acid; the latter can be obtained from it:



$$(CH_3)_2CO \xrightarrow{CHCl_3} (CH_3)_2C{<}{CCl_3 \atop OH} \longrightarrow (CH_3)_2C{<}{CO_2H \atop OH}$$

Trichloro-*tert.*-butyl alcohol. α-Hydroxy*iso*butyric acid.

(25) Ketones can be alkylated by the use of sodamide and alkyl iodides (see p. 258, method (11)).

Metal ketyls, see Vol. II.

Acetone, *Dimethyl ketone* [Propanone], $CH_3{\cdot}CO{\cdot}CH_3$, is isomeric with propionaldehyde, propylene oxide, trimethylene oxide, and allyl alcohol. It occurs in small quantities in the blood and normal urine, whilst in the urine of those suffering from diabetes it is present in considerable amount, due to the breaking down of the acetoacetic acid formed at first. It is also produced in the dry distillation of tartaric acid, citric acid (*q.v.*), sugar, cellulose (wood), and is, therefore, found in crude wood spirit (p. 136). Technically it is prepared by the distillation of calcium acetate, or from crude wood spirit. More recently it has been obtained on a technical scale by the fermentation of starch and sugar-containing materials by suitable bacteria (*Bacillus Macerans, Bacterium acetoethylicum*) (Chem. Ztg. **1926,** 257).

It is also formed by the usual methods: by the oxidation of *iso*propyl alcohol, *iso*butyric acid, and α-hydroxy*iso*butyric acid; by heating ββ-dichloro- and -dibromopropane, $CH_3CX_2CH_3$, with water to 160–180°; and β-chloro- and β-bromopropylene, $CH_3CX{=}CH_2$, with water at 200°. The alcohol, $CH_3{\cdot}C(OH):CH_2$, first formed undergoes isomerization to acetone. Acetone is similarly formed from allylene, $CH_3{\cdot}C:CH$, by action of sulphuric acid or $HgBr_2$ in the presence of water (p. 112).

It results, further, in the action of zinc methyl on acetyl chloride; and, accompanied by diacetyl, by the electrolysis of a solution of pyroracemic acid and potassium acetate (Ber. **33**, 650). Acetone is also formed from α-bromo*iso*butyric amide by bromine and alkali (C. 1905, I. 1219):

$$(CH_3)_2CBr{\cdot}CONHBr \xrightarrow{2KOH} (CH_3)_2CO + NH_3 + 2KBr + CO_2.$$

(See also the general methods of formation of the ketones, pp. 256–258.)

Acetone is a mobile, peculiar-smelling liquid, b.p. 56·5°, m.p. — 94°, D_{20} 0·7920. It is miscible with water, alcohol, and ether. Calcium chloride, or potassium carbonate, throws it out from its aqueous solution.

It is an excellent solvent for many carbon compounds, and for many inorganic salts such as potassium permanganate, etc. (Ber. **37,** 4328). Its most important reactions, such as its behaviour on reduction, its reactions with amyl nitrite, bisulphites, ammonia, hydroxylamine, phenylhydrazine, etc., have been described under the general reactions of the ketones. The sodium derivative of β-allyl alcohol, $CH_3{\cdot}C(ONa):CH_2$, appears to be formed by the action of sodium (Ann. **278,** 116).

By passing acetone vapour, diluted with nitrogen, through a tube at a dark-red heat, methane and keten are formed (Ber. **43,** 2821. See p. 270):

$$CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow CH_4 + CH_2:CO.$$

Detection and Estimation of Acetone.—Acetone is most readily detected by the iodoform reaction, iodoform being readily produced by the action of iodine and a weak alkali on acetone (see p. 291). Acetone can be quantitatively determined by means of mercuric sulphate (Ber. **32**, 986); also by heating it with mercuric acetate, whereby acetone-mercury substitution compounds are produced (Ber. **36**, 3699). Mercuric oxide dissolves in a weakly alkaline aqueous solution of acetone, forming the compound $2C_3H_6O{\cdot}3HgO$ which by boiling with alkalis changes to the insoluble acetone mercarbide, $CH_3COCHg_3O_2H$ (Ber. **38**, 2677).

Other reactions for the detection of acetone, see Ber. **17**, R. 503 : **18**, R. 195 : Ann. **223**, 143 : Atti. R. Accad. Lincei. [5] **22**, I. 376.

Acetone is used for the manufacture of sulphonal (p. 267), chloroform (p. 290) and iodoform (p. 291). During the war it was largely used for the manufacture of *iso*prene (Merling. Z. angew. Chem. **34**, 403).

Homologues of Acetone.—(*a*) Simple ketones are usually prepared by the distillation of the calcium or barium salts of the corresponding fatty acids.

Name.	Formula.	M.P.	B.P.
Diethyl ketone, Propione	$CO(C_2H_5)_2$	—	103°
Di-*n*-propyl ketone, Butyrone	$CO(C_3H_7)_2$	—	144°
Di-*iso*propyl ketone, Tetramethylacetone	$CO[CH(CH_3)_2]_2$	—	124°
Di-*iso*butyl ketone, *iso*Valerone	$CO[CH_2CH(CH_3)_2]_2$	—	165°
n-Caprone	$CO(C_5H_{11})_2$	14·6°	226°
Tetraethylacetone	$CO[CH(C_2H_5)_2]_2$	—	203°
Œnanthone	$CO(C_6H_{13})_2$	30°	263°
Caprylone	$CO(C_7H_{15})_2$	40°	—
Caprinone	$CO(C_8H_{17})_2$	48°	—
Laurone	$CO(C_{11}H_{23})_2$	69°	—
Myristone	$CO(C_{13}H_{27})_2$	76°	—
Palmitone	$CO(C_{15}H_{31})_2$	83°	—
Stearone	$CO(C_{17}H_{35})_2$	88°	—

Diethyl ketone is produced from carbon monoxide and potassium ethyl (p. 223). *Tetramethyl-* and *tetraethylacetone* have been obtained as decomposition products of pentamethyl- and pentaethyl-phloroglucinol, when these bodies were oxidized by air (Ber. **25**, R. 504).

(*b*) *Mixed Ketones.*—The majority of these compounds have been prepared by the distillation of a mixture of barium acetate with the barium salt of another fatty acid. Many have also been prepared by the useful reaction between acid chlorides and alkyl zinc iodides (Bull. Soc. Chim. [4], **9**, 1):

$$R{\cdot}CO{\cdot}Cl + R'ZnI \longrightarrow R{\cdot}CO{\cdot}R' + ZnClI.$$

Name.	Formula.	M.P.	B.P.*
Methyl ethyl ketone	$CH_3{\cdot}CO{\cdot}C_2H_5$	—	81°
Methyl propyl ketone	$CH_3{\cdot}CO{\cdot}C_3H_7$	—	102°
Methyl *iso*propyl ketone	$CH_3{\cdot}CO{\cdot}CH(CH_3)_2$	—	96°
Methyl *sec.*-butyl ketone	$CH_3{\cdot}CO{\cdot}CH_2CH(CH_3)_2$	—	116°
Pinacolin, Methyl *tert.*-butyl ketone	$CH_3{\cdot}CO{\cdot}C(CH_3)_3$	—	106°
Methyl hexyl ketone	$CH_3{\cdot}CO{\cdot}C_6H_{13}$	—	171°
Methyl heptyl ketone	$CH_3{\cdot}CO{\cdot}C_7H_{15}$	− 15°	193°
Methyl nonyl ketone	$CH_3{\cdot}CO{\cdot}C_9H_{19}$	+ 15°	225°
Methyl decyl ketone	$CH_3{\cdot}CO{\cdot}C_{10}H_{21}$	21°	247°
Methyl undecyl ketone	$CH_3{\cdot}CO{\cdot}C_{11}H_{23}$	28°	263°
Methyl dodecyl ketone	$CH_3{\cdot}CO{\cdot}C_{12}H_{25}$	34°	(207°)
Methyl tridecyl ketone	$CH_3{\cdot}CO{\cdot}C_{13}H_{27}$	39°	(224°)
Methyl tetradecyl ketone	$CH_3{\cdot}CO{\cdot}C_{14}H_{29}$	43°	(231°)
Methyl pentadecyl ketone	$CH_3{\cdot}CO{\cdot}C_{15}H_{31}$	48°	(244°)
Methyl hexadecyl ketone	$CH_3{\cdot}CO{\cdot}C_{16}H_{33}$	52°	(252°)
Methyl heptadecyl ketone	$CH_3{\cdot}CO{\cdot}C_{17}H_{35}$	55°	(265°)

* Boiling points in parentheses determined at 100 mm.

Methyl ethyl ketone occurs in crude wood spirit.

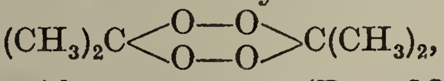
Methyl iso*propyl ketone* is formed by several reactions involving the migration of a methyl group. Thus it is formed by the action of strong sulphuric acid on trimethyllactic acid, $CMe_3 \cdot CHOH \cdot CO_2H$ (Ber. **25**, R. 905), from *tert.*-butylcarbinol, $CMe_3 \cdot CH_2OH$, along with trimethylacetaldehyde by oxidation with chromic acid (Ann. **351**, 260) and from ββ-dimethyltrimethylene glycol, $CMe_2(CH_2OH)_2$, by dehydration (C. 1900, II. 32).

Methyl sec.-*butyl ketone* is obtained from methacrylic esters, $CH_2 : CMe \cdot CO_2Et$ and two molecules of magnesium methyl iodide. (C. 1907, I. 559).

Pinacolin is obtained by the withdrawal of water from *pinacone*, tetramethylethylene glycol, $(CH_3)_2C(OH) \cdot C(OH)(CH_3)_2$, and from trimethylacetyl chloride and zinc methyl (p. 257). When oxidized with chromic acid, it breaks down into trimethylacetic and formic acid. Potassium permanganate converts it into trimethylpyroracemic acid (*q.v.*). It is converted by methyl iodide and sodamide into *ethyl* tert.-*butyl ketone*, $CMe_3 \cdot CO \cdot CH_2Me$, b.p. 125°, iso*propyl* tert.-*butyl ketone* (pentamethylacetone), $CMe_3 \cdot CO \cdot CHMe_2$, b.p. 134°, and *di*-tert.-*butyl ketone*, $CMe_3 \cdot CO \cdot CMe_3$ (*pivalone*), b.p. 150° (Compt. rend. **150**, 582). Reduction yields pinacolyl alcohol (p. 149): for further reactions, see C. 1906, II. 496.

Homologous pinacolins are obtained from other polysubstituted glycols. Thus, *methyl* tert.-*amyl ketone*, $CMe_2Et \cdot CO \cdot Me$, b.p. 130·6°, is obtained from the glycol $CMe_2OH \cdot CMeEtOH$, and *ethyl* tert.-*amyl ketone*, $CMe_2Et \cdot CO \cdot Et$, b.p. 151°, from the two glycols $CMeEtOH \cdot CMeEtOH$ and $CMe_2OH \cdot CEt_2OH$ (Ann. **396**, 208).

Methyl nonyl ketone is the chief constituent of oil of rue (from *Ruta graveolens*), from which it may be extracted by shaking with concentrated sodium bisulphite solution (C. 1902, I. 744). *Methyl heptyl ketone* occurs in the same oil (C. 1901, I. 1006; 1903, I. 29; Ber. **35**, 3587).

Acetone Peroxides.—Two cyclic acetone peroxides are known. cyclo-*Diacetone peroxide*,  $(CH_3)_2C \langle \begin{smallmatrix} O-O \\ O-O \end{smallmatrix} \rangle C(CH_3)_2$, m.p. 132°, is prepared by the action of H_2SO_5 (Caro's acid) on acetone (Ber. **33**, 858). cyclo-*Triacetone peroxide*, $(C_3H_6O_2)_3$, m.p. 97°, is obtained from acetone and hydrogen peroxide, with special ease when in the presence of hydrochloric acid. It is insoluble in water, but soluble in benzene and in ether. It forms beautiful crystals, and explodes when struck or suddenly heated (Ber. **28**, 2265). Methyl ethyl ketone and H_2SO_5 produce methyl ethyl ketone peroxide, $(C_4H_8O_2)_2$, a colourless oil, which explodes above 100° (C. 1907, I. 944).

1. HALOGEN SUBSTITUTION PRODUCTS OF THE KETONES

Monochloroacetone, $CH_3 \cdot CO \cdot CH_2Cl$, b.p. 119°, is obtained when chlorine is conducted into cold acetone (Ann. **279**, 313), preferably in the presence of marble (Ber. **26**, 597); also by the electrolysis of a mixture of acetone and hydrochloric acid (C. 1902, I. 101). Its vapours provoke tears. *Oxime*, b.p. 71°/9 mm.

as- or α-*Dichloroacetone*, $CH_3 \cdot CO \cdot CHCl_2$, b.p. 120°, is formed on treating warmed acetone with chlorine, and is also obtained from dichloroacetoacetic ester (Ber. **15**, 1165). sym.- or β-*Dichloroacetone*, $ClCH_2 \cdot CO \cdot CH_2Cl$, m.p. 45°, b.p. 172–174°, is obtained by the chlorination of acetone and in the oxidation of α-dichlorohydrin, $CH_2Cl \cdot CH(OH) \cdot CH_2Cl$ (*q.v.*), with potassium dichromate and sulphuric acid.

sym.-*Tetrachloroacetone*, $CHCl_2 \cdot CO \cdot CHCl_2 + 2H_2O$, m.p. 48–49°, is obtained by the action of potassium chlorate and hydrochloric acid on chloroanilic acid (Ber. **21**, 318) and triaminophenol (Ber. **22**, R. 666); or of chlorine on phloroglucinol (Ber. **22**, 1478). unsym.-*Tetrachloroacetone*, $CH_2Cl \cdot CO \cdot CCl_2$, b.p. 183°, is produced by the action of chlorine on *iso*propyl alcohol (C. 1897, I. 28).

Pentachloroacetone, $CHCl_2 \cdot CO \cdot CCl_3$, b.p. 193°, is obtained from chlorine and acetone (Ann. **279**, 317).

Monobromoacetone, $CH_2Br \cdot CO \cdot CH_3$, b.p. 31°/8 mm. (Ber. **29**, 1555: **31**, 2684). *Oxime*, m.p. 36°. *Pentabromoacetone*, m.p. 74°, is produced from acetone dicarboxylic acid and bromine (C. 1899, I. 596). *Perbromoacetone*, $CBr_3 \cdot CO \cdot CBr_3$, m.p. 110–111°, is obtained from triaminophenol (Ber. **10**, 1147), and bromoanilic acid (Ber. **20**, 2040; **21**, 2441) by means of bromine and water.

Iodoacetone, $CH_3 \cdot CO \cdot CH_2I$, b.p. 58°/11 mm., is produced when potassium iodide in an aqueous methyl alcohol solution acts on monochloroacetone (Ber. **29**, 1557). It is a heavy oil with an intolerable pungent odour. *Oxime*, m.p. 64°.

β-Di-iodoacetone, $CH_2I{\cdot}CO{\cdot}CH_2I$, results when iodine chloride acts on acetone.

Methyl β-chloroisobutyl ketone, $(CH_3)_2{\cdot}CCl{\cdot}CH_2{\cdot}CO{\cdot}CH_3$, and *di-β-chloro*iso*butyl ketone*, $(CH_3)_2CCl{\cdot}CH_2{\cdot}CO{\cdot}CH_2CCl(CH_3)_2$, are the readily decomposable addition products of mesityl oxide and phorone with hydrochloric acid.

Methyl ω-bromobutyl ketone, $CH_2Br(CH_2)_3{\cdot}CO{\cdot}Me$, b.p. 216°, is obtained from hydrobromic acid and acetobutyl alcohol.

γγ′-Dibromoketones are prepared from the oxetones (cyclic anhydrides of the γγ′-dihydroxyketones, *q.v.*) by the action of hydrobromic acid, *e.g. γγ-dibromobutyl ketone*, $(CH_3CHBr{\cdot}CH_2{\cdot}CH_2)_2CO$, is formed from dimethyl oxetone and 2HBr, or by the addition of 2HBr to diallyl acetone (p. 276). **αα-Dichloroketones** are discussed with the diketones.

2. KETONE ACETALS

The ketones may be regarded as the anhydrides of hypothetical glycols, which bear the same relation to the ketones that the orthocarboxylic acids do to the carboxylic acids. In this sense it is then permissible to speak of ortho-ketones. Their alkyl ethers, corresponding with the acetals, are produced by heating the β-diethoxy-carboxylic acids, and also from acetone by means of orthoformic ester (*Claisen*, Ber. **31**, 1010):

$$CH_3{\cdot}C(OC_2H_5)_2CH_2{\cdot}CO_2H \longrightarrow CH_3{\cdot}C(OC_2H_5)_2{\cdot}CH_3 + CO_2$$
$$CH_3{\cdot}CO{\cdot}CH_3 + HC(OC_2H_5)_3 \longrightarrow CH_3{\cdot}C(OC_2H_5)_2CH_3 + HCO_2C_2H_5.$$

Acetone dimethyl acetal, $(CH_3)_2C(OCH_3)_2$, b.p. 83°. *Acetone diethyl acetal*, b.p. 114°, is a liquid with an odour resembling that of camphor. These substances are stable when pure, but water or a trace of mineral acid causes them to break down into ketones and alcohols.

The ortho-esters of higher acids react on ketones like the first member, and the same may be said of the imido-ether hydrochloride and alcohol mixture. *Methyl ethyl ketone diethyl acetal*, b.p. 120°; *diethyl ketone diethyl acetal*, b.p. 154°; *dipropyl ketone diethyl acetal*, b.p. 70°/12 mm., are prepared from acetimido-ether hydrochloride or phenyl acetimido-ether hydrochloride and alcohol (Ber. **40**, 3020).

3. KETONE HALIDES

These are produced, as mentioned on p. 261, by the action of PCl_5, PCl_3Br_2, and PBr_5 upon ketones. They easily give up halogen acid by the action of alkalis, forming halogen-olefines (p. 122), which in turn yield acetylene.

Acetone chloride, ββ-Dichloropropane, $CH_3{\cdot}CCl_2{\cdot}CH_3$, b.p. 70°; $D_{16} = 1{\cdot}827$. *ββ-Dibromopropane*, b.p. 114°; $D_0 = 1{\cdot}8149$. *ββ-Dichlorobutane*, $CH_3{\cdot}CCl_2{\cdot}C_2H_5$, b.p. 96°. *ββ-Dibromobutane*, b.p. 144°. *ββ-Dichloro-γγ-dimethylbutane*, $CH_3{\cdot}CCl_2{\cdot}C(CH_3)_3$, is produced from pinacolin by PCl_5 (comp. C. 1906, II. 496). *Heptachloropropane*, $CHCl_2{\cdot}CCl_2{\cdot}CCl_3$, m.p. 30°, b.p. 150°, is obtained from pentachloroacetone (Ann. **297**, 314).

4. KETONE BISULPHITES AND SULPHOXYLATES

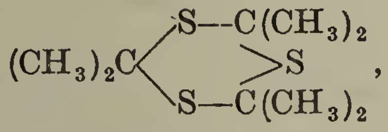
The addition compounds, which ketones containing a methyl group form with alkali bisulphites, comparably with the aldehydes, are probably salts of hydroxysulphonic acids (see p. 244):

$$RR'{\cdot}C(OH)SO_3Na.$$

With alkali cyanides they yield hydroxy-acid nitriles (C. 1903, I. 1244). Reduction produces ketone sulphoxylates, $(CH_3)_2C(OH){\cdot}OSONa$, which are also formed, together with bisulphites, from ketones and hydrosulphites (C. 1907, I. 855; 1909, I. 1208: Ber. **59**, 2341).

5. SULPHUR DERIVATIVES OF THE SATURATED KETONES

A. **Thioketones and their Sulphones.**—When hydrogen sulphide acts on a cold mixture of acetone and concentrated hydrochloric acid, the first product is a volatile body with an exceedingly disagreeable odour which spreads with great rapidity. It is probably thioacetone, which has not been further investigated. The final product of the reaction is—

Trithioacetone,  $(CH_3)_2C\langle\begin{smallmatrix}S-C(CH_3)_2\\ \rangle S\\ S-C(CH_3)_2\end{smallmatrix}$, m.p. 24°, b.p. 130°/13 mm.

Potassium permanganate oxidizes it to the *trisulphone*, $[(CH_3)_2CSO_2]_3$, m.p. 302°. When distilled at the ordinary pressure it is converted into *dithioacetone*, $(CH_3)_2C{<}\begin{smallmatrix}S\\S\end{smallmatrix}{>}C(CH_3)_2$, b.p. 183–185°. This is also formed in the action of phosphorus trisulphide on acetone. It is converted, by oxidation, into the *disulphone*, $[(CH_3)_2CSO_2]_2$, m.p. 220–225°.

Methyl ethyl ketone behaves similarly (C. 1903, II. 281).

B. **Mercaptoles and their Sulphones.**—Although the ketone derivatives corresponding with the acetals cannot be derived from ketones and alcohols by the withdrawal of water, it is possible to obtain the *mercaptoles*—the ketone derivatives corresponding with the mercaptals—in this manner; but best, however, by the action of hydrochloric acid on ketones and mercaptans:

$$(CH_3)_2CO + 2C_2H_5SH \xrightarrow{HCl} (CH_3)_2C(SC_2H_5)_2 + H_2O.$$

Like the mercaptals, they are liquids with unpleasant odour.

Acetone ethyl mercaptole, $(CH_3)_2C(SC_2H_5)_2$, b.p. 190–191°, may be prepared from mercaptan. However, to avoid the intolerable odour of the latter, sodium ethyl thiosulphate and hydrochloric acid are used (p. 176). It combines with methyl iodide (Ber. **19**, 1787: **22**, 2592). By this means, from a series of simple and mixed ketones, corresponding mercaptoles have been made, and in nearly all instances they have been oxidized to the corresponding sulphones, some of which possess medicinal value.

Sulphonal, *Acetone diethyl sulphone*, $(CH_3)_2C(SO_2C_2H_5)_2$, m.p. 126°, was discovered by *Baumann*, and was introduced into medicine, as a very active sleep-producing agent, by *Kast* in 1888. It is prepared by oxidation of acetone mercaptole with potassium permanganate:

$$(CH_3)_2{\cdot}C(SC_2H_5)_2 \xrightarrow{4O} (CH_3)_2{\cdot}C(SO_2C_2H_5)_2.$$

It is also formed by the action of sodium hydroxide and methyl iodide (Ann. **253**, 147) on ethylidene diethyl sulphone (p. 247):

$$CH_3CH(SO_2C_2H_5)_2 \xrightarrow{NaOH} CH_3{\cdot}CNa(SO_2C_2H_5)_2 \xrightarrow{CH_3I} (CH_3)_2C(SO_2C_2H_5)_2.$$

Trional, *Methyl ethyl ketone diethyl sulphone*, $\begin{smallmatrix}CH_3\\C_2H_5\end{smallmatrix}{>}C(SO_2C_2H_5)_2$, m.p. 75°; **tetronal,** *pentane-γγ-diethyl sulphone*, $(C_2H_5)_2C(SO_2C_2H_5)_2$, m.p. 85°; *pentane-γγ-dimethyl sulphone*, $(C_2H_5)_2C(SO_2CH_3)_2$, m.p. 132–133°, and other "*sulphonals*," are prepared similarly to sulphonal, and act in like manner. However, acetone dimethyl sulphone, $(CH_3)_2C(SO_2CH_3)_2$, not containing an ethyl group, no longer acts like sulphonal as a soporific.

6. NITROGEN DERIVATIVES OF THE KETONES

A. **Nitro Compounds.**—The *pseudo*nitroles, $RR'C(NO){\cdot}NO_2$, and *gem.*-dinitro compounds, $RR'C(NO_2)_2$, have already been discussed (p. 184).

B. The compounds which acetone forms with **ammonia,** *diacetoneamine* and *triacetoneamine*, are discussed in detail later (p. 274). From some of the higher ketones, ammonia produces products of the type $RR'C(N:CRR')_2$ from which the original ketone can be easily regenerated (C. 1905, II. 540: 1907, I. 810).

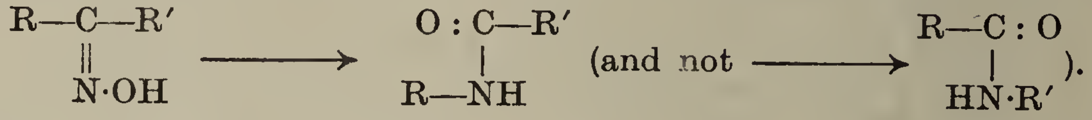
C. **Hydroxylamine Derivatives.—Ketoximes** (*V. Meyer*). In general, the ketoximes are formed with greater difficulty than the aldoximes (Ber. 39, 1452: C. 1905, I. 1219). It is usually best to apply the hydroxylamine in a strongly alkaline solution (Ber. **22**, 605: Ann. **241**, 187: C. 1908, I. 937). They are also produced when the *pseudo*nitroles are reduced by free hydroxylamine or potassium hydrosulphide (Ber. **28**, 1367 : **29**, 87, 98), or by the reduction of secondary nitroparaffins by stannous chloride and HCl.

They are very similar in properties to the aldoximes. Acids resolve them into their components, whilst sodium amalgam and acetic acid convert them into primary amines (p. 190). They are characteristically distinguished from the aldoximes by their behaviour towards acid chlorides or acetic anhydride, yielding in part acid esters ; and by their conversion by the same reagents, as well as by HCl or H_2SO_4 in glacial acetic acid, into acid amides (*Beckmann transformation*, Ber. **20**, 506, 2580 : comp. also Ber. **24**, 4018 : Ann. **312, 172**, note).

$$\begin{matrix}CH_3\\CH_3CH_2CH_2\end{matrix}\!\!>C{=}NOH \longrightarrow CH_3CO{\cdot}NHCH_2CH{\cdot}CH_3.$$

Methyl propyl ketoxime. Acetopropylamide.

The mechanism of the Beckmann transformation has been largely studied by Meisenheimer, particularly in connection with the aromatic and mixed aliphatic-aromatic ketones (Ann. **446**, 205). He has shown that, contrary to the previously accepted mechanism, the alkyl group which stands *anti-* to the OH group migrates to the nitrogen :



$$\begin{array}{c}R{-}C{-}R'\\ \|\\ N{\cdot}OH\end{array} \longrightarrow \begin{array}{c}O:C{-}R'\\ |\\ R{-}NH\end{array} \quad \text{(and not} \longrightarrow \begin{array}{c}R{-}C:O\\ |\\ HN{\cdot}R'\end{array}\text{).}$$

Nitrogen tetroxide converts the ketoximes into *pseudonitroles* (p. 184). Chlorine and sodium hydroxide or bromine and pyridine produce chloro- and bromo-nitrosoparaffins (p. 182).

Ketoximes combine with hydrocyanic acid to form nitriles of α-hydroxylamino-carboxylic acids (Ber. **29**, 62).

Acetoxime, $(CH_3)_2C : NOH$, m.p. 59–60°, b.p. 135°, smells like chloral. It dissolves readily in water, alcohol, and ether, from which it crystallizes well (Ber. **20**, 1505 : **39**, 876).

The hydroxyl hydrogen present in acetoxime may be replaced by acid radicals through the agency of acid chlorides or anhydrides (Ber. **24**, 3537).

Methyl ethyl ketoxime, b.p. 152°. *Methyl* n-*propyl ketoxime*, b.p. 168° (C. 1898, II. 474), is an oil with an agreeable odour. *Methyl* iso*propyl ketoxime*, b.p. 157°. *Methyl* n-*butyl ketoxime*, b.p. 185°. *Methyl* tert.-*butyl ketoxime* (Pinacolin oxime), m.p. 75°, reacting with PCl_5 produces aceto-*tert.*-butylamine. Nitrogen tetroxide does not produce a *pseudo*nitrole, but a nitrimine, $C(CH_3)_3{\cdot}C(CH_3) : N{\cdot}NO_2$, or the tautomer $C(CH_3)_3C(: CH_2){\cdot}N : NOOH$. (Comp. mesityl nitrimine, p. 275, and Ann. **338**, 1.)

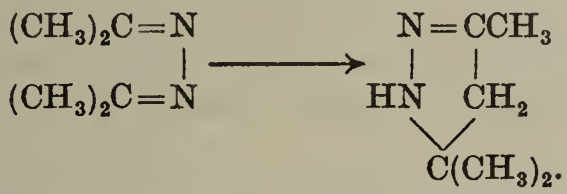
n-*Butyrone oxime*, b.p. 193°. iso*Butyrone oxime*, m.p. 6–8°, b.p. 181–185°. *Methyl nonyl ketoxime*, m.p. 42°, under the influence of concentrated sulphuric acid, forms considerable quantities of capric methylamide, $C_9H_{19}CONHCH_3$, together with acetononylamide (Ber. **35**, 3592). *Capryl ketoxime*, m.p. 20°. *Nonyl ketoxime*, m.p. 12°. *Lauryl ketoxime*, $(C_{11}H_{23})_2C : N{\cdot}OH$, m.p. 39°. *Myristyl ketoxime*, $(C_{13}H_{27})_2C : N{\cdot}OH$, m.p. 51°. *Palmityl ketoxime*, $(C_{15}H_{31})_2C : N{\cdot}OH$, m.p. 59°. *Stearyl ketoxime*, $(C_{17}H_{35})_2C : N{\cdot}OH$, m.p. 62°.

D. Hydrazine Derivatives.—The first product of excess of hydrazine in the cold on ketones is the production of the unstable ketone hydrazones, which on standing split off hydrazine with the formation of the very stable ketazines (Ber. **25**, R. 80) :

$$2RR'CO + 2NH_2{\cdot}NH_2 \longrightarrow 2RR'C : N{\cdot}NH_2 \longrightarrow RR'C : N{\cdot}N : CRR' + NH_2{\cdot}NH_2$$

The ketazines are also formed by direct combination between two molecules of ketone and one of hydrazine. They are hydrolysed to the ketone and hydrazine by acids, but are stable to alkalis. When heated with sodium ethoxide, the ketone hydrazones break down into nitrogen and a paraffin (Ann. **394**, 86) (Curtius and Thun).

Dimethyl ketazine in contact with acids changes into the isomeric trimethylpyrazoline (Ber. **27**, 770: C. 1901, II. 1121):



The homologous methylalkylketazines behave similarly, whilst diethylketazine does not undergo the change (C. 1898, II. 1249).

Diethylketazine, however, is converted on heating with zinc chloride into 3 : 4-dimethyl-2 : 5-diethylpyrrole (Ber. **43**, 493):

Acetone hydrazone, $Me_2C:N{\cdot}NH_2$, b.p. 124°.

Dimethyl ketazine, $Me_2C:N{\cdot}N:CMe_2$, b.p. 131°, *methyl ethyl ketazine,* b.p. 170°, *methyl propyl ketazine,* b.p. 197°, *methyl hexyl ketazine,* b.p. 290°, *diethyl ketazine,* b.p. 193°.

E. Ketone Phenylhydrazones (E. Fischer, Ber. **16**, 661 : **17**, 576 : **20**, 513 : **21**, 984).—These compounds result by the action of phenylhydrazine on the ketones. They behave like the aldehyde phenylhydrazones, and form indole derivatives when heated with HCl or $ZnCl_2$.

Acetone phenylhydrazone, $(CH_3)_2C:N_2HC_6H_5$, m.p. 16°, b.p. 165°/93 mm.

Methyl n-*propyl ketone phenylhydrazone,* b.p. 206°/100 mm.

p-**Nitrophenylhydrazones** are specially suitable for identifying ketones on account of the relative insolubility of the compound formed. *Acetone* p-*nitrophenylhydrazone,* $(CH_3)_2C:NNHC_6H_4NO_2$, m.p. 148° (C. 1904, I. 14).

F. Ketone semicarbazones result when ketones are mixed with semicarbazide, $NH_2CO{\cdot}NH{\cdot}NH_2$ (*q.v.*) at ordinary temperatures. Such compounds are particularly suitable for the identification of the ketones, on account of the excellent way they crystallize.

Acetone semicarbazone, $(CH_3)_2C:NNHCONH_2$, m.p. 187°. *Methyl ethyl ketone semicarbazone,* m.p. 135°. *Diethyl ketone semicarbazone,* m.p. 139°, and other members, see Ber. **34**, 2123.

3B. UNSATURATED KETONES AND KETENS

(*a*) KETENS, RR′C : CO *

The ketens discovered by Staudinger in 1905 are a special type of unsaturated ketone of the general formula RR′C : CO. The simplest keten, $CH_2:CO$, was prepared by Wilsmore in 1907 by the action of a red-hot platinum wire on acetone, acetic anhydride and acetic ester (J.C.S. **91**, 1938). Keten bears the same relation to acetic acid as carbon monoxide to formic acid, and can be regarded as an internal anhydride of acetic acid. The acetals corresponding to the keten hydrates (tautomeric with the carboxylic acids), $RR'C:C(OR'')_2$, are known.

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* H. Staudinger, Die Ketene (Stuttgart, 1912, Enke).

In the presence of two adjacent double bonds, $R_2C : C : O$, ketens resemble such compounds as the *iso*cyanic esters, $R \cdot N : C : O$, and Staudinger proposed, on account of the similarity in formula and reactions of such compounds, to class them together under the name *carbonylenes.* Regarding the aliphatic diazo compounds as possessing an open chain formula (but see p. 251), he grouped these with these compounds under the proposed name *azenes* (Helv. Chim. Acta. **5,** 86).

Ketens of the type $RCH : CO$ are known as *aldoketens,* those containing two alkyl groups, $RR'C : CO$, as *ketoketens.*

Formation.—(1) By the action of zinc on α-bromo-fatty acid bromides in indifferent solvents :

$$CH_2Br \cdot COBr \xrightarrow{Zn} CH_2{=}CO + ZnBr_2$$
$$(CH_2)_2CBr \cdot CBr \xrightarrow{Zn} (CH_3)_2C{=}CO + ZnBr_2.$$

(2) By the pyrogenic decomposition of acetone (Ber. **43,** 2821) or acetic anhydride :

$$CH_3 \cdot CO \cdot CH_3 \longrightarrow CH_4 + CH_2 : CO$$
$$(CH_3 \cdot CO)_2O \longrightarrow H_2O + 2CH_2 : CO.$$

(3) By heating dialkyl malonic anhydrides (Ber. **41,** 2208 : Helv. Chim. Acta. **6,** 291) :

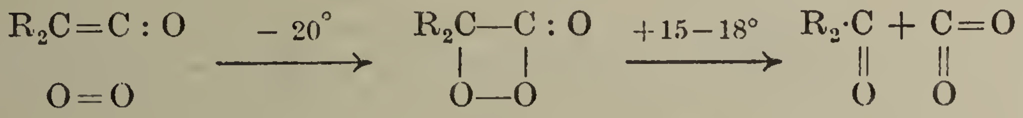
(4) By heating certain diazomethane derivatives, *e.g.* diazodesoxybenzoin (Schroeter : see Vol. II) :

$$C_6H_5 \cdot CO \cdot C(: N_2) \cdot C_6H_5 \longrightarrow N_2 + C_6H_5 \cdot CO \cdot C(C_6H_5){<} \longrightarrow (C_6H_5)_2C : CO.$$

Properties.—The aldoketens are colourless, and usually very unstable. The ketoketens are more stable and are yellow in colour, the depth of colour depending upon the nature of the two alkyl groups. The ketens show no carbonyl reactions, but, on the other hand, manifest great additive capacity at the C : C linking. They behave as internal anhydrides of the fatty acids in their addition reactions with water, alcohols, amines, halogen hydrides and fatty acids, with the formation respectively of fatty acids, esters, amides, acid halides and mixed acid anhydrides. It cannot be definitely stated whether the addition takes place first at the C : O linking, with subsequent isomerization, or whether the addition takes place directly at the C : C linking.

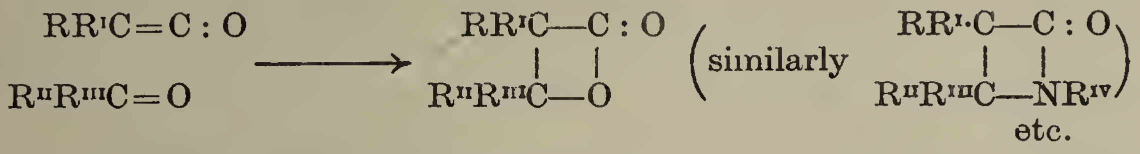
The extraordinary reactivity of the adjacent double linkages leads to spontaneous polymerization, very often very suddenly, this tendency being particularly marked with the aldoketens and leading to difficulties in their preparation in a pure condition (Ber. **49,** 2697 : **53,** 1073, 1917 : Helv. Chim. Acta. **7,** 3). In some cases, the original form can be recovered by distillation of the dimeric product.

The ketens are extraordinarily sensitive to atmospheric oxygen. They combine with oxygen in solution to moloxides, which are stable at a low temperature, but which decompose at room-temperature into ketones and CO_2. In the dry state they are explosive (Ber. **58**, 1079):



$$\begin{array}{c}R_2C{=}C:O\\ O{=}O\end{array} \xrightarrow{-20^\circ} \begin{array}{c}R_2C\text{—}C:O\\ |\quad\ |\\ O\text{—}O\end{array} \xrightarrow{+15-18^\circ} \begin{array}{ccc}R_2\cdot C & + & C{=}O\\ \| & & \|\\ O & & O\end{array}$$

Ketens add themselves to the unsaturated linkages C : C, N : N, N : O, C : O, C : N (Ber. **44,** 521 : Helv. Chim. Acta. **7,** 8). Their union with carbonyl compounds and Schiff's bases to form the otherwise difficultly accessible β-lactones and β-lactams is important (Ber. **50,** 1035). The stability of the so-formed ring compounds is discussed in Helv. Chim. Acta. **5,** 3 :



$$\begin{array}{c}RR^{I}C{=}C:O\\ R^{II}R^{III}C{=}O\end{array} \longrightarrow \begin{array}{c}RR^{I}C\text{—}C:O\\ |\quad\ |\\ R^{II}R^{III}C\text{—}O\end{array} \left(\text{similarly}\quad \begin{array}{c}RR^{I}\cdot C\text{—}C:O\\ |\quad\ |\\ R^{II}R^{III}C\text{—}NR^{IV}\end{array}\right)$$

etc.

Ketens also combine with CO_2 with the formation of dicarboxylic anhydrides (see preparation, method (3)) (Helv. Chim. Acta. **8,** 306).

Tertiary bases such as pyridine and quinoline form the so-called keten bases with two molecules of dimethylketen. With stronger tertiary bases such as triethylamine, ketinium compounds containing one mol. of keten to one mol. of base are formed (Ber. **42,** 1271).

Keten, $CH_2 : CO$, m.p. − 151°, b.p. − 56°, is colourless, poisonous and has an odour of chlorine and acetic anhydride (Ber. **41**, 594). *Methylketen,* CHMe : CO (Ber, **41,** 906 : **44,** 533), and *ethylketen* have only been obtained in ethereal solution.

Dimethylketen, $CMe_2 : CO$, m.p. − 97·5°, b.p. 34°, is a mobile light-yellow liquid which polymerizes at ordinary temperature to tetramethyl*cyclo*butanedione (Ber. **39**, 968 : **40**, 1149). *Diethylketen,* b.p. 92°, is obtained from diethylmalonic anhydride (Ber. **41,** 2208).

Carbon suboxide, CO : C : CO, which is closely related to the ketens, is dealt with later, in connection with malonic acid.

Keten Acetals.—The keten acetals, $R_2C : C(OR')_2$, are obtained by the action of water on the reaction product of sodamide on acetic ester (Scheibler *et al.*, Ann. **458,** 21 : see under acetoacetic ester).

Keten diethyl acetal, $CH_2 : C(OEt)_2$, b.p. 78°, is a colourless liquid with a faint ethereal odour, readily soluble in organic solvents and to an appreciable extent in water. On hydrolysis it yields acetic ester and alcohol, and by the action of bromine, bromoacetic ester and ethyl bromide.

*Keten di-*n*-propyl acetal,* b.p. 104–106° ; *diisobutyl acetal,* b.p. 110–112° ; *diisoamyl acetal,* b.p. 131–133°.

Methylketen diethyl acetal, CHMe : $C(OEt)_2$, b.p. 78–81°, is obtained from ethyl propionate.

(*b*) OLEFINE AND DIOLEFINE KETONES

Olefine ketones, in which the double bond is situated next to the keto-group, are very easily prepared, and are interesting in their behaviour.

(1) (*a*) $\alpha\beta$-olefine ketones are obtained from the product of condensation of ketones with aldehydes or ketones ; the keto-alcohols which are formed easily give up water :

$$CH_3CHO + CH_3COCH_3 \rightarrow CH_3CH(OH)CH_2COCH_3 \rightarrow CH_3CH : CHCOCH_3.$$

Condensation of several molecules of the same ketone results in the formation of αβ-olefine ketones and diolefine ketones : *e.g.* acetone yields mesityl oxide and phorone :

$$2CH_3COCH_3 \longrightarrow (CH_3)_2C : CHCOCH_3 \xrightarrow{(CH_3)_2CO} (CH_3)_2C : CHCOCH : C(CH_3)_2$$

(*b*) The β-halogen ketones, which are readily obtained by the condensation of β-halogen fatty acid chlorides and zinc alkyls, lose halogen hydride and yield αβ-unsaturated ketones when treated with diethylaniline (C. 1906, I. 650 : 1908, I, 1913) :

$$X\cdot CH_2\cdot CH_2\cdot COCl \xrightarrow{ZnEt_2} X\cdot CH_2\cdot CH_2\cdot CO\cdot Et \longrightarrow CH_2 : CH\cdot CO\cdot Et.$$

(*c*) The αβ-unsaturated ketones are obtained by condensing olefines with acid chlorides in the presence of aluminium chloride (C. 1910, I. 1335 ; *cf.* Ber. **27**, R. 941) :

$$Me_2C : CH_2 + CH_3\cdot COCl \longrightarrow Me_2C : CH\cdot CO\cdot CH_3.$$

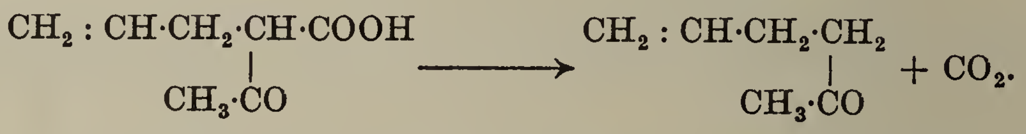
This may be regarded as a special example of the very important Friedal-Crafts reaction for the preparation of many aromatic compounds.

(*d*) In some cases αβ-unsaturated ketones are obtained by condensing Δ^α-unsaturated acid chlorides with zinc alkyl iodides (Ann. Chim. Phys. [8] **15**, 556).

(2) Allyl alkyl ketones can be prepared from the acid nitriles, allyl iodide and zinc. They very easily change into propenyl alkyl ketones, under the influence of mineral acids (C. 1905, I. 431) :

$$CH_2C : N \xrightarrow{C_3H_5ZnI} CH_3COCH_2CH : CH_2 \longrightarrow CH_3COCH : CHCH_3.$$

(3) Unsaturated ketones with any desired position of the double bond can be obtained by hydrolysis of β-ketonic esters or β-diketones containing the appropriate unsaturated group. Thus, allylacetoacetic ester yields methyl Δ^γ-butenyl ketone (allylacetone) :



$$\begin{array}{c} CH_2 : CH\cdot CH_2\cdot CH\cdot COOH \\ | \\ CH_3\cdot CO \end{array} \longrightarrow \begin{array}{c} CH_2 : CH\cdot CH_2\cdot CH_2 \\ | \\ CH_3\cdot CO \end{array} + CO_2.$$

The αβ-unsaturated ketones show very marked additive properties at the C : C linkage adjacent to the carbonyl group. On reduction, they yield according to the conditions saturated ketones or saturated alcohols. The reduction to the unsaturated alcohol has not yet been accomplished (Ann. **330**, 212). By the use of aluminium amalgam dimolecular condensation products are also formed (Ann. **296**, 295). On the other hand, the unsaturated ketones with separated double bonds yield exclusively the unsaturated alcohol when reduced with sodium and alcohol.

Semicarbazide yields the semicarbazidosemicarbazones, $R\cdot CH(NH\cdot NH\cdot CO\cdot NH_2)\cdot CH_2\cdot C(: N\cdot NH\cdot CO\cdot NH_2)\cdot R'$, as well as the normal semicarbazone (Ber. **40**, 4764). *Hydroxylamine* produces not only oximes but also β-hydroxylamino-oximes, $RCH(NHOH)\cdot CH_2C(: NOH)R$. *Ammonia*, primary and secondary *amines* are particularly easily taken up, forming β-aminoketones. *Hydrazines* react with the CO and C=C groups, producing cyclic pyrazolines.

Mercaptans form not only mercaptoles, but also mercapto-mercaptoles, even when the C=C group is not contiguous to the CO group ; *e.g.* :

$CH_3CH(SC_2H_5)CH_2C(SC_2H_5)_2CH_3$, $CH_3CH(SC_2H_5)CH_2CH_2C(SC_2H_5)_2CH_3$,

etc. In phorone, only the two C=C groups react, yielding :

$(CH_3)_2C(SC_2H_5)\cdot CH_2\cdot CO\cdot CH_2C(SC_2H_5)(CH_3)_2$ (Ber. **37**, 502).

Sulphurous and hydrocyanic acids sometimes unite with the C=C group rather than with the CO. Malonic ester, acetoacetic ester, and other such reactive bodies similarly unite with the C=C bond of αβ-olefine ketones, forming $RCOCH_2CR\cdot CH(CO_2C_2H_5)_2$, etc.

Addition compounds with the halogen acids are very readily formed. It is a general rule that, when HX becomes attached to these unsaturated substances, the hydrogen atom always takes the α- position to the CO group and the X group the β- position.

Bromine forms αβ-dibromoparaffin ketones which readily give up HBr, leaving α-bromo-olefine ketones, which yield α-diketones on hydrolysis (Ber. **34**, 2092).

Methyl vinyl ketone (*Methyleneacetone*) $CH_2 : CH\cdot CO\cdot Me$, b.p. 80°, is a strongly refracting, very pungent oil obtained from acetonylcarbinol, $CH_3\cdot CO\cdot CH_2\cdot CH_2OH$, or β-acetylacrylic acid, $CH_3\cdot CO\cdot CH : CH\cdot CO_2H$, by distillation under ordinary pressure. *Methyl* iso*propenyl ketone*, $CH_2 : CMe\cdot CO\cdot Me$, b.p. 96°, is obtained similarly (D.R.P. 222551, 227176, 242612 ; C. 1910, II. 120, 1421 : 1912, I. 385). They polymerize very easily.

Ethyl-, *propyl-*, and iso*butyl-vinyl ketones*, b.p. 31°/47 mm., 24°/10 mm. and 32°/10 mm. are obtained by loss of HCl from the corresponding alkyl β-chloroethyl ketones.

Methyl allyl ketone, b.p. 108°, *ethyl allyl ketone*, b.p. 127°, and *propyl allyl ketone*, b.p. 147°, $CH_2 : CH\cdot CH_2COR$, are readily changed by mineral acids into *methyl propenyl ketone*, b.p. 121°, *ethyl propenyl ketone*, b.p. 137°, and *propyl propenyl ketone*, b.p. 157°.

Ethylideneacetone, $CH_3CH{=}CH\cdot CO\cdot CH_3$, b.p. 121°. It has a penetrating odour like that of crotonaldehyde. It is formed when hydracetylacetone (*q.v.*) is boiled with acetic anhydride or anhydrous oxalic acid (Ber. **25**, 3166 : **34**, 2092). iso*Butylideneacetone*, $(CH_3)_2CH\cdot CH : CH\cdot COCH_3$, b.p. 51°/16 mm. (C. 1900, I. 403). iso*Amylideneacetone* $(CH_3)_2CH\cdot CH_2CH : CHCOCH_3$, b.p. 180° (Ber. **27**, R. 121 ; C. 1897, I. 365). *Heptachloroethylideneacetone*, $CHCl_2CCl{=}CCl\cdot CO\cdot CCl_3$, b.p. 184°/14 mm., results when trichloroacetyltetrachlorocrotonic acid is heated with water (Ber. **25**, 2695).

Mesityl oxide, $(CH_3)_2C{=}CH\cdot CO\cdot CH_3$, b.p. 130°, is a liquid smelling like peppermint. **Phorone**, $(CH_3)_2C{=}CH\cdot CO\cdot CH{=}C(CH_3)_2$, m.p. 28°, b.p. 196°. These are formed simultaneously on treating acetone with dehydrating agents, *e.g.* $ZnCl_2$, H_2SO_4, and HCl. Hydrochloric acid is best adapted for this purpose, the acetone being saturated with it, while it is cooled. The addition products which are first formed, $(CH_3)_2CCl\cdot CH_2\cdot COCH_3$ and $(CH_3)_2CCl\cdot CH_2\cdot CO\cdot CH_2\cdot CCl(CH_3)_2$, are decomposed by alkali hydroxides, and the mesityl oxide and phorone then separated by distillation. When acetone is condensed by lime or sodium ethylate there is produced along with the mesityl oxide a cyclic ketone isomeric with phorone, called iso*phorone* (Vol. II).

The diacetone alcohol which is formed as an intermediate product readily decomposes when heated with a little concentrated sulphuric acid into mesityl oxide and water (Monatsh. **34**, 779). The formation of mesityl oxide is reversible. By shaking with 1% HCl mesityl oxide takes up water and forms diacetone alcohol : concentrated acids, or warming with dilute sulphuric acid split it into two molecules of acetone. Phorone is similarly broken down when heated with dilute sulphuric acid (Ann. **180**, 1).

Mesityl oxide takes up two atoms of bromine, and phorone four.

Phorone tetrabromide, $CMe_2Br\cdot CHBr\cdot CO\cdot CHBr\cdot CMe_2Br$, m.p. 89° (Ann. **180**, 21) yields when heated with alcoholic potassium acetate or pyridine, *αα-dibromophorone*, $CMe_2 : CBr\cdot CO\cdot CBr : CMe_2$, m.p. 30° (Ann. **406**, 154). *Ozonides of mesityl oxide and phorone*, and their breakdown products, see Ann. **374**, 338.

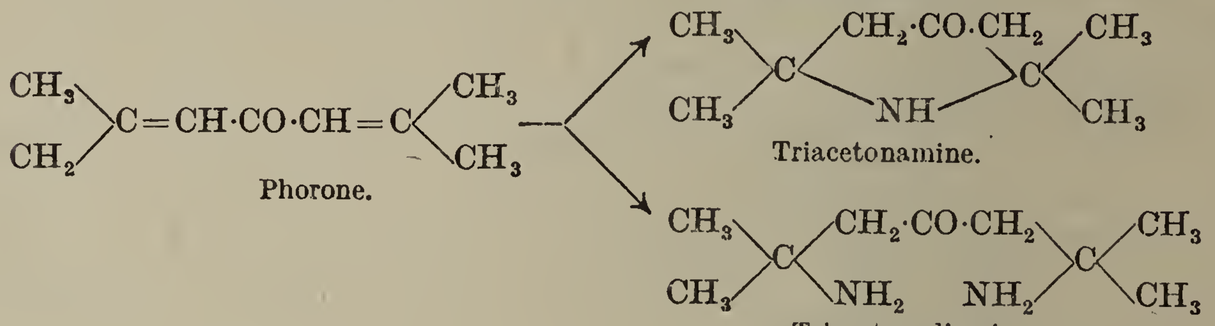
Just as acetone condenses to mesityl oxide and phorone, so the homologous ketones, and methyl ethyl ketone, methyl propyl ketone, methyl heptyl ketone, and methyl nonyl ketone are condensed by hydrochloric acid (Ber. **36**, 2555) or zinc chloride, and acetyl chloride (C. 1903, II. 566) or calcium carbide (C. 1909, II. 1421) to homologues of mesityl oxide and phorone.

Historical.—*Kane* discovered mesityl oxide in 1838, when he obtained it, together with mesitylene, by the action of concentrated sulphuric acid on acetone. At that time he regarded acetone as alcohol, and called it mesitalcohol. In mesityl oxide and mesitylene, Kane thought he had discovered bodies which bore the same relation to mesityl alcohol or acetone that ethyl ether or ethyl oxide and ethylene bear to ethyl alcohol. *Kekulé* developed the formula $(CH_3)_2{\cdot}C{=}CH{\cdot}CO{\cdot}CH_3$ for mesityl oxide, which was substantiated later by *Claisen*. *Baeyer* discovered phorone, and *Claisen* assigned to it the formula $(CH_3)_2C{=}CH{\cdot}CO{\cdot}CH{=}C(CH_3)_2$ (Ann. **180**, 1).

The Action of Ammonia on Acetone and Mesityl Oxide and Phorone

Ammonia unites with mesityl oxide and phorone at their double bonds and forms three bases, diacetonamine, triacetonamine, and triacetonediamine—the same that are formed from ammonia and acetone (*Heintz*, Ann. **174**, 133 : **198**, 42 : **203**, 336). There are two possible courses that the reaction may follow: firstly, that the acetone is condensed to mesityl oxide and phorone by the ammonia which then become converted into the amines, or secondly, the ammonia forms a simple addition compound, $(CH_3)_2C<^{OH}_{NH_2}$, which then condenses.

Mesityl oxide. Diacetonamine.



Phorone. Triacetonamine.

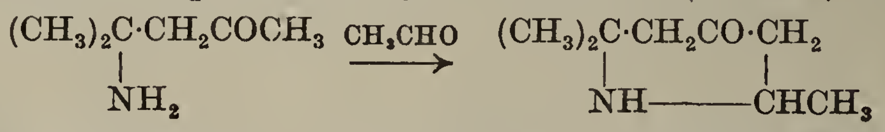
Triacetonediamine.
(Ann. **203**, 336).

Diacetonamine forms a colourless liquid, slightly soluble in water, which is decomposed into mesityl oxide and ammonia by distillation (Ber. **7**, 1387). It shows a strongly alkaline reaction and forms crystalline salts with one equivalent of acid. The *hydrochloride*, acted on by potassium nitrite, yields diacetone alcohol, $(CH_3)_2C(OH)CH_2COCH_3$ (*q.v.*), which can be considered to be a derivative of diacetonamine. It loses water and changes to mesityl oxide. Urea derivative of diacetonamine, see Ber. **27**, 377. *Diacetonamine oxime*, m.p. 55°, b.p. 121°/12 mm. (Ber. **34**, 300, 792).

Oxidation by chromic acid mixture produces α-amino-*iso*butyric acid, $(CH_3)_2C(NH_2)COOH$, and β-amino-*iso*valeric acid, $(CH_3)_2C(NH_2){\cdot}CH_2COOH$.

Triacetonamine, m.p. 39·6°; $+1H_2O$, m.p. 58°, is prepared from phorone and ammonia, and is a secondary base (p. 187). It crystallizes anhydrous in needles, and with one molecule of water in large quadratic tables. It is weakly alkaline. Its hydrochloride with potassium nitrite yields a *nitrosamine*, $C_9H_{16}ON{\cdot}NO$, m.p. 73°, which regenerates phorone when boiled with sodium hydroxide. The nitroso-body is transformed by hydrochloric acid back into triacetonamine. This substance, with bromine, forms N-*bromotriacetonamine*, $C_9H_{16}ONBr$, m.p. 44° (Ber. **31**, 668). For further reactions, see Vol. II.

Phorone and primary amines produce N-*methyltriacetonamine*, etc. (Ber. **28**, R. 166). Just as the reaction of diacetonamine with acetone yields triacetonamine, so acetaldehyde produces vinyldiacetonamine (Ber. **17**, 1788).



$$\underset{\displaystyle NH_2}{(CH_3)_2C}{\cdot}CH_2COCH_3 \xrightarrow{CH_3CHO} (CH_3)_2C{\cdot}CH_2CO{\cdot}CH_2 \;/\; NH{-}CHCH_3$$

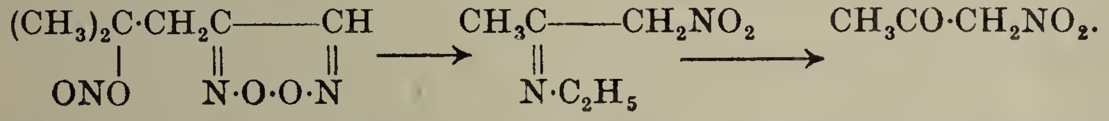
With cyanoacetic ester an analogous δ-lactam is formed (Ber. **26**, R. 450).

Action of Hydroxylamine and Semicarbazide on Mesityl Oxide and Phorone

According to the conditions of experiment, hydroxylamine becomes added on to the mesityl oxide molecule and gives diacetonehydroxylamine, or else oxime formation takes place. In the case of phorone, however, only addition compounds are formed—triacetone hydroxylamine and triacetone dihydroxylamine, corresponding with the two compounds obtained with ammonia.

Mesityl oxide oxime, $(CH_3)_2C{=}CH{\cdot}C(NOH)CH_3$, α-form, b.p. 83°/9 mm., β-form, m.p. 49°, b.p. 92°/9 mm., is prepared from mesityl oxide and free hydroxylamine. It is obtained in two modifications. The oily α-oxime is transformed into the solid β-form by the action of heat on the hydrochloride, or by repeated distillation under reduced pressure. The latter, boiled with alkali, regenerates the α-modification.

Mesityl nitrimine, $(CH_3)_2C{=}CH{\cdot}C{<}\begin{smallmatrix}CH_3\\ N\cdot NO_2\end{smallmatrix}$, m.p. 155°, with violent decomposition, is produced when both modifications of mesityl oxide oxime are treated with amyl nitrite in glacial acetic acid (Ber. **32**, 1336). Reduction changes it to *trimethylpyrazoline* (Vol. III). Heated with water it forms an isomeric *trimethylisoxazolone oxime* (Vol. III); oxidation with nitric acid changes it to *nitritomesityl dioxime peroxide*. This is converted by aniline in glacial acetic acid solution into anilonitro-acetone, which, in turn, is changed by sulphuric acid into *nitro-acetone* (Ann. **319**, 230).



$$\begin{matrix}(CH_3)_2C\cdot CH_2C & \text{———} & CH \\ | \quad\quad\quad \| & & \| \\ ONO \quad\; N\cdot O\cdot O\cdot N & & \end{matrix} \longrightarrow \begin{matrix}CH_3C\text{———}CH_2NO_2 \\ \| \\ N\cdot C_2H_5\end{matrix} \longrightarrow CH_3CO\cdot CH_2NO_2.$$

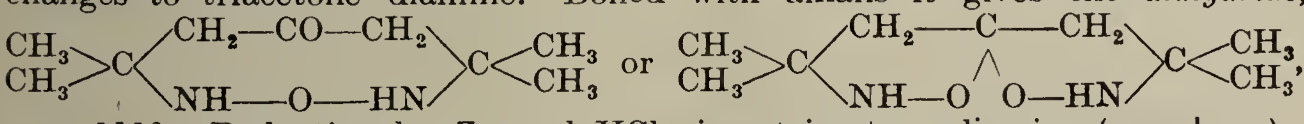
Diacetone hydroxylamine, $\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_2COCH_3\\ NHOH\end{smallmatrix}$, m.p. 52°, b.p. 95°/10 mm., is formed, together with α-mesityl oxide oxime, by the action of free hydroxylamine on mesityl oxide. Oxidation with chromic acid yields:

β-Nitroso-iso*propylacetone*, $\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_2-CO-CH_3\\ NO\end{smallmatrix}$, dimolecular form, m.p. 75°; monomolecular form, b.p. 60°/11 mm., which is also formed from diacetonamine (p. 274) by oxidation with persulphuric acid. In the *dimolecular* condition it forms white tabular crystals, which melt to a blue *monomolecular* liquid. It is easily decomposed (comp. nitrosoparaffins, p. 183, and Ber. **36**, 1069).

β-Nitro-iso*propylacetone*, $(CH_3)_2C(NO_2)CH_2COCH_3$, b.p. 119°/17 mm., is produced when diacetone hydroxylamine is oxidized with nitric acid. It can be reduced back to its parent compound by aluminium amalgam (Ber. **36**, 158).

Triacetonehydroxylamine, $\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_2-CO-CH_2\\ \text{——}N(OH)\text{——}\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}$, m.p. 50°, is prepared from phorone and hydroxylamine hydrochloride, and yields with hydroxylamine, an *oxime*, m.p. 126°.

Triacetonedihydroxylamine, $\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_2-CO-CH_2\\ NHOH\quad HOHN\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}$, m.p. 113°, b.p. 135°/20 mm. (Ber. **36**, 657), results from interaction of phorone and two molecular proportions of free hydroxylamine. Reduced by Zn and HCl, it changes to triacetone diamine. Boiled with alkalis it gives the *anhydride*,



$$\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_2-CO-CH_2\\ NH\text{——}O\text{——}HN\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix} \text{ or } \begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_2\text{——}C\text{——}CH_2\\ \wedge \\ NH-O\quad O-HN\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix},$$

m.p. 111°. Reduction by Zn and HCl gives triacetone diamine (see above).

*Dinitrosodi*iso*propylacetone*, $\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_2-CO-CH_2\\ NO\qquad\quad ON\end{smallmatrix}{>}C{<}\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}$, m.p. 132°, is produced from triacetone dihydroxylamine by chromic acid (Ber. **31**, 1379). On melting it forms a deep-blue liquid.

Semicarbazide derivatives.—*Mesityl oxide semicarbazone*, $Me_2C:CH{\cdot}C(:N{\cdot}NH{\cdot}CO{\cdot}NH_2)CH_3$, m.p. 156°, is obtained from mesityl oxide and semicarbazide in neutral or alkaline solution. In acid solution, on the other hand, the *compound* $Me_2C(NH{\cdot}NH{\cdot}CO{\cdot}NH_2)CH_2{\cdot}C(:N{\cdot}NH{\cdot}CO{\cdot}NH_2)CH_3$, m.p. 221°, is obtained. The semicarbazide residue attached to the ketonic carbon atom can be removed by benzaldehyde with the formation of *mesityl oxide semicarbazide*,

$Me_2C(NH{\cdot}NH{\cdot}CO{\cdot}NH){\cdot}CH_2{\cdot}CO{\cdot}CH_3$. Under certain conditions a *compound*, m.p. 131°, isomeric with the semicarbazone can be obtained. This is probably a pyrazoline derivative (Ber. **36**, 4377 : **42**, 4503 : J.C.S. **103**, 377).

Allyl acetone, $CH_2 : CH{\cdot}CH_2{\cdot}CH_2COCH_3$, is obtained from allyl acetoacetic ester. It is isomeric with mesityl oxide (C. 1898, II. 663 : Ber. **33**, 1472).

Methylheptenone, $(CH_3)_2C{=}CH{\cdot}CH_2{\cdot}CH_2COCH_3$, b.p. 173°, is found in a number of ethereal oils which contain citral, linalool, and geraniol. It results from the distillation of cineolic anhydride (Vol. II). Synthetically it can be produced by the action of sodium hydroxide solution on the reaction product of sodium acetylacetone and amylene dibromide, $(CH_3)_2CBr{\cdot}CH_2CH_2Br$ (Ber. **29**, R. 590). It is also prepared from dimethylallylacetoacetic ester, the result of the reaction between acetoacetic ester and amylene dibromide, and sodium ethoxide solution (Ber. **34**, 594). It possesses a penetrating odour like amyl acetate. Oxidation with $KMnO_4$ breaks it down to acetone and lævulinic acid ; zinc chloride produces dihydro-*m*-xylene (Ann. **258**, 323 : Ber. **28**, 2115, 2126).

$\Delta^{\beta\delta}$-*Octadien*-ζ-*one.—Sorbic ethyl ketone*, $CH_3{\cdot}CH : CH{\cdot}CH : CH{\cdot}CO{\cdot}C_2H_5$, b.p. 93°/26 mm., is prepared from sorbyl chloride and zinc ethyl (Ber. **34**, 2222).

Condensation of the respective $\alpha\beta$-olefine aldehydes (p. 253) with acetone leads to the formation of the following diolefine ketones (Ber. **28**, R. 608 : C. 1906, II. 1112) :

(1) γ-*Methyl*-$\Delta^{\beta\delta}$-*octadien*-ζ-*one*, $CH_3CH : C(CH_3)CH : CHCOCH_2$, b.p. 92°/12 mm.

(2) δ-*Methyl*-$\Delta^{\gamma\epsilon}$-*nonadien*-η-*one*, $(CH_3)CH_2CH : C(CH_3)CH : CHCO{\cdot}CH_3$, b.p. 97°/8 mm.

(3) β-*Methyl*-ϵ-iso*propyl*-$\Delta^{\delta\zeta}$-*decadien*-ι-*one*, $(C_3H_7)CH_2CH : C(C_3H_7)CH : CH{\cdot}COCH_3$.

Boiling with zinc chloride gives rise to benzene derivatives with varying facility : (1) no condensation ; (2) a bad yield ; (3) a better one (see Vol. II).

Diallylacetone, $CH_2{=}CH{\cdot}CH_2{\cdot}CH_2COCH_2{\cdot}CH_2{\cdot}CH{=}CH_2$, b.p. 116°/70 mm., is prepared from diallylacetone carboxylic ester (comp. Oxetone).

pseudo-*Ionone* is also a diolefine ketone, and is described in Vol. II, together with the olefine terpenes.

(*c*) ACETYLENE KETONES

These are obtained by the action of acid chlorides on sodium compounds of alkyl acetylene.

Acetylœnanthylidene, $CH_3[CH_2]_4C{\equiv}C{\cdot}COCH_3$, b.p. 93°/18 mm., is obtained from sodium œnanthylidene and acetyl chloride. It possesses an irritating odour. Dilute H_2SO_4 converts it into acetyl caproyl methane, $CH_3[CH_2]_4CO{\cdot}CH_2COCH_3$ (C. 1900, II. 1231, 1262). Hydroxylamine and hydrazines combine with the acetylene ketones, forming isoxazoles and pyrazoles respectively (C. 1903, II. 122 : 1904, I. 43).

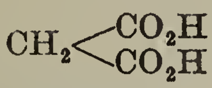
4. MONOBASIC CARBOXYLIC ACIDS

The organic acids are characterized by the group, ·CO·OH, called carboxyl, of which the hydrogen can be replaced by metals and alcohol radicals, forming salts and esters.

The number of carboxyl groups present in them determines their basicity, and distinguishes them as mono-, di-, tri-basic, etc., or as mono-, di-, and tri-carboxylic acids :

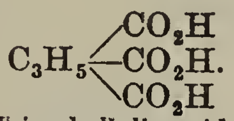
$CH_3{\cdot}CO_2H$

Acetic acid (monobasic).



$CH_2{<}\genfrac{}{}{0pt}{}{CO_2H}{CO_2H}$

Malonic acid (dibasic).



$C_3H_5\begin{cases}CO_2H\\CO_2H.\\CO_2H\end{cases}$

Tricarballylic acid (tribasic).

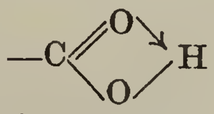
According to Hantzsch (Ber. **50**, 1422) the old formulation of the carboxyl group as $—C{\lessdot}\genfrac{}{}{0pt}{}{O}{OH}$ is unsatisfactory. According to him, two forms of the carboxyl group are to be recognized :

I. Derivatives of the *pseudo*carboxylic acids, $R{\cdot}C{\lessdot}\genfrac{}{}{0pt}{}{O}{OH}$ from which the non-dissociating esters are derived.

II. Derivatives of the true carboxylic acids $R{\cdot}C{<}\genfrac{}{}{0pt}{}{O}{O}\Big\}H$ from which the salts $R{\cdot}C{<}\genfrac{}{}{0pt}{}{O}{O}\Big\}M$ are derived.

In the free carboxylic acids an equilibrium exists between the two forms, determined by their dissociation and the solvent in which they are dissolved.

In the second form, the hydrogen atom is linked to the two oxygen atoms in the second sphere by two subsidiary ionized valencies in Werner's scheme. The great mobility of the hydrogen atoms in the acids and the metallic atoms in the salts is thus explained. The view of Hantzsch is further supported by the totally different optical behaviour of the esters on the one hand and the salts on the other.

The evidence, however, seems opposed to the view that the formula of the carboxyl group could be represented as  which is the electronic representation of Werner's type II (see Sidgwick, *Electronic Theory of Valency*, Oxford, 1927, p. 252).

The saturated monobasic acids can be looked on as being combinations of the carboxyl group with alcohol radicals ; they are ordinarily termed fatty acids. They correspond with the saturated primary alcohols and aldehydes.

The unsaturated acids of the acrylic acid and propiolic acid series, corresponding with the unsaturated primary alcohols and aldehydes, are derived from the fatty acids by the loss of two and four hydrogen atoms.

The following classes will be described:

A. *Paraffin monocarboxylic acids*, $C_nH_{2n}O_2$, formic acid or acetic acid series. (Fatty acids.)

B. *Olefine monocarboxylic acids*, $C_nH_{2n-2}O_2$, oleic or acrylic acid series.

C. *Acetylene monocarboxylic acids*, $C_nH_{2n-4}O_2$, propiolic acid series.

D. *Diolefine carboxylic acids*, $C_nH_{2n-4}O_2$.

Nomenclature.—The "Geneva nomenclature" deduces the names of the carboxylic acids from the corresponding hydrocarbons; thus formic acid is [methane acid] and acetic acid is [ethane acid], etc.

The *radical* of the acid is the residue in combination with the hydroxyl group:

$CH_3\cdot CO—$	$CH_3\cdot CH_2\cdot CO—$	$CH_3\cdot CH_2\cdot CH_2\cdot CO—$
Acetyl.	Propionyl.	Butyryl.

The names of the trivalent hydrocarbon residues, which in the acid residues are united with oxygen, are indicated by the insertion of the syllable "en" into the names of the corresponding alcohol radicals:

$CH_3\cdot C\equiv$	$CH_3\cdot CH_2\cdot C\equiv$	$CH_3\cdot CH_2\cdot CH_2\cdot C\equiv$
Ethenyl.	Propenyl.	*n*-Butenyl.

The group $CH\equiv$ is called the methenyl group or the methine group.

Derivatives of the Monocarboxylic Acids.—Numerous classes of bodies can be derived by changes in the carboxyl group. In connection with the fatty acids mention will only be made of the salts. The other classes of derivatives will be considered separately after the fatty acids themselves. They are:

(1) *Esters*, resulting from the replacement of hydrogen in the carboxyl group by alcohol radicals (p. 310).

(2) *Chlorides* (bromides, iodides, and fluorides), which are compounds of the acid radicals with the halogens (p. 314).

(3) *Acid anhydrides* (p. 317), compounds of the acid radicals with oxygen.

(4) *Acid peroxides* (p. 319).

(5) *Thio-acids* (p. 319).

(6) *Carbithionic acids.*

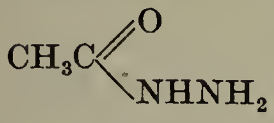
(7) *Acid amides* (p. 321), compounds of the acid radicals with NH_2.

(8) *Acid nitriles* (p. 324).

Hence acetic acid yields the following:

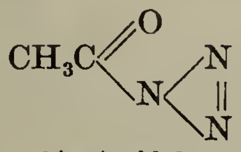
$CH_3\cdot CO_2\cdot C_2H_5$	$CH_3\cdot COCl$	$(CH_3\cdot CO)_2O$	$(CH_3\cdot CO)_2O_2$
Ethyl acetate.	Acetyl chloride.	Acetic anhydride.	Acetyl peroxide.
$CH_3\cdot COSH$	$CH_3\cdot CSSH$	$CH_3\cdot CONH_2$	$CH_3\cdot C\equiv N.$
Thioacetic acid.	Methyl carbithionic acid.	Acetamide.	Acetonitrile.

The less important derivatives of the fatty acids belong to the following classes, which will be described later :



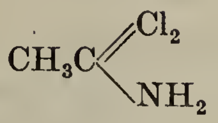
$CH_3C\begin{matrix}\diagup\!\!\diagup O \\ \diagdown NHNH_2\end{matrix}$

Acetohydrazide.



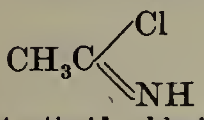
$CH_3C\begin{matrix}\diagup\!\!\diagup O \\ \diagdown N\begin{matrix}\diagup N \\ \| \\ \diagdown N\end{matrix}\end{matrix}$

[Acetazide].



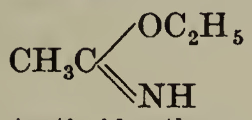
$CH_3C\begin{matrix}\diagup\!\!\diagup Cl_2 \\ \diagdown NH_2\end{matrix}$

Acetamide chloride.



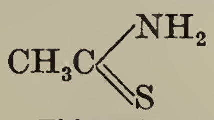
$CH_3C\begin{matrix}\diagup Cl \\ \diagdown\!\!\diagdown NH\end{matrix}$

Acetimide chloride.



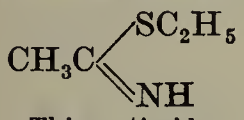
$CH_3C\begin{matrix}\diagup OC_2H_5 \\ \diagdown\!\!\diagdown NH\end{matrix}$

Acetimido-ether.



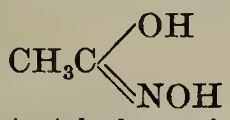
$CH_3C\begin{matrix}\diagup NH_2 \\ \diagdown\!\!\diagdown S\end{matrix}$

Thioacetamide.



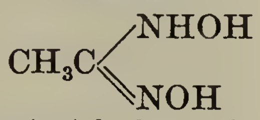
$CH_3C\begin{matrix}\diagup SC_2H_5 \\ \diagdown\!\!\diagdown NH\end{matrix}$

Thioacetimido ether.



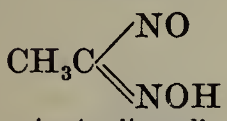
$CH_3C\begin{matrix}\diagup OH \\ \diagdown\!\!\diagdown NOH\end{matrix}$

Acetohydroxamic acid.



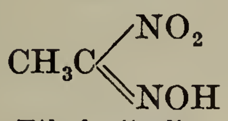
$CH_3C\begin{matrix}\diagup NHOH \\ \diagdown\!\!\diagdown NOH\end{matrix}$

Acetohydroxamic oxime.



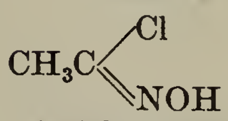
$CH_3C\begin{matrix}\diagup NO \\ \diagdown\!\!\diagdown NOH\end{matrix}$

Acetonitrosolic acid.



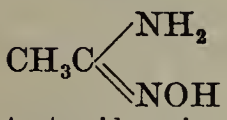
$CH_3C\begin{matrix}\diagup NO_2 \\ \diagdown\!\!\diagdown NOH\end{matrix}$

Ethyl nitrolic acid.



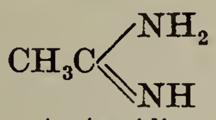
$CH_3C\begin{matrix}\diagup Cl \\ \diagdown\!\!\diagdown NOH\end{matrix}$

Acetohydroximic acid chloride.



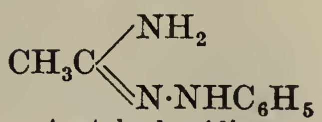
$CH_3C\begin{matrix}\diagup NH_2 \\ \diagdown\!\!\diagdown NOH\end{matrix}$

Acetamide oxime.



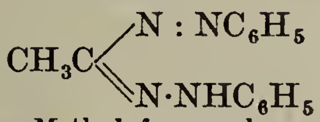
$CH_3C\begin{matrix}\diagup NH_2 \\ \diagdown\!\!\diagdown NH\end{matrix}$

Acetamidine.



$CH_3C\begin{matrix}\diagup NH_2 \\ \diagdown\!\!\diagdown N{\cdot}NHC_6H_5\end{matrix}$

Acetohydrazidine.



$CH_3C\begin{matrix}\diagup N : NC_6H_5 \\ \diagdown\!\!\diagdown N{\cdot}NHC_6H_5\end{matrix}$ etc.

Methyl formazyl.

Aromatic carboxylic acids, especially benzoic acid, are particularly suitable for the preparation of carboxylic acid derivatives, and various classes of substances which actually belong here, have been discovered and more closely studied in the aromatic series. Benzoic acid transmits its own facility in crystallization to its derivatives, so that the process of investigation becomes the easier.

Similarly, the aromatic amines and hydrazines, such as aniline, toluidine, and phenylhydrazine, are more easily prepared and more convenient to manipulate than the corresponding aliphatic compounds, so that in this direction also the benzene derivatives have been more closely investigated than the simple methane compounds.

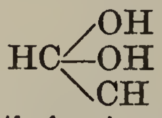
Numerous derivatives are also obtained by the replacement of the hydrogen atoms in the radical combined with hydroxyl by other atoms or groups. The halogen substitution products will be described under the fatty acids, after the discussion of the various classes mentioned in the preceding paragraphs.

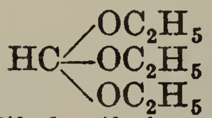
The fatty acids can be recovered from all of the above classes of derivatives by simple reactions.

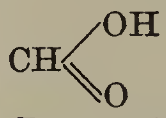
It has already been indicated under the oxygen derivatives of the methane hydrocarbons, that aldehydes, ketones, and carboxylic acids may be considered to be anhydrides of theoretical, non-existing dihydric or trihydric alcohols, in which the hydroxyl groups are attached to the same carbon atom (p. 46).

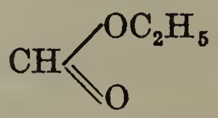
The trihydric alcohols, corresponding with the carboxylic acids, do not exist, but ethers of them are known, as are the ethers derived from the hydrated forms of the aldehydes (acetals, p. 241). The hypothetical, trihydric alcohols, of which the carbonic acids may be considered anhydrides, have been called *ortho acids*, just as tribasic phosphoric acid is termed orthophosphoric acid (Ann. **139**, 114 : Jahresbericht. 1859, 152 : Ber. **2**, 115). This designation has also been applied to the orthoaldehydes and orthoketones.

It is customary, therefore, to speak of orthoformic esters (the esters of tribasic formic acid), and of *formic acid* (which, in view of the relation of orthophosphoric to metaphosphoric acid, PO(OOH), might be termed metaformic acid) and of *formic acid esters* :

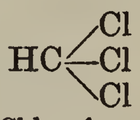

[Orthoformic acid.] Unknown.

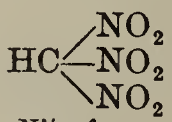

Ethyl orthoformate.

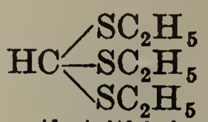

Formic acid.


Ethyl formate.

The chloride, bromide, and iodide corresponding with orthoformic acid are chloroform, bromoform, and iodoform ; further derivatives are nitroform and orthotrithioformic ester :


Chloroform.


Nitroform.


Ethyl orthotrithioformate.

The ortho-acid derivatives will be discussed immediately following the derivatives of ordinary formic acid.

Comparably to the above, substances are known which are derived from orthoacetic acid, $CH_3C(OH)_3$:

$CH_3C(OC_2H_5)_3$	CH_3CCl_3	$CH_3C(NO_2)_3$	$CH_3C(NC_5H_{10})_3$
Ethyl orthoacebate.	Methyl chloroform.	Methyl nitroform.	Orthoacetic piperidide.

In many reactions of the carboxylic acids and their derivatives (esterification, hydrolysis of esters, amides, acid chlorides, etc.), the ortho-acid derivatives play an important part as unstable intermediate compounds.

A. MONOBASIC SATURATED ACIDS, PARAFFIN MONOCARBOXYLIC ACIDS, $C_nH_{2n+1}·CO_2H$

Formic acid, H·CO·OH, is the first member of this series. The radical HCO, which, here, is united to hydroxyl, is called *formyl.* This acid is distinguished from all its homologues and the unsaturated monocarboxylic acids, in that it exhibits not only the character of a monobasic acid, but also that of an aldehyde. To express in a name its aldehyde character the acid might be designated *hydroxyformaldehyde,* HO·CHO.

FORMIC ACID AND ITS DERIVATIVES

It is not only the aldehyde character which distinguishes formic acid from acetic acid and its homologues, but also the absence of a chloride and anhydride, corresponding with acetyl chloride and acetic anhydride (*q.v.*). The withdrawal of water from formic acid leads to the formation of carbon monoxide, a reaction which does not take place in the case of any of the higher homologues. (Compare, however, the ketens, which may be regarded as internal anhydrides of the fatty acids.) Hydrocyanic acid, the nitrile of formic acid, has an acid nature, and therein differs from the indifferent nitriles of the homologous acids. Formic acid is twelve times stronger than acetic acid, as is shown by the dissociation constants (*Ostwald*).

Carbon monoxide, and its nitrogen-containing derivatives, the iso-

nitriles or *carbylamines*, C=N—R′, and *fulminic acid*, C=NOH, will be described after formic acid.

Formic acid, H·CO·OH [Methane acid], is found free in ants, in the procession caterpillar, *Bombyx processionea*, in pine needles, and in various animal secretions (perspiration), from all of which it may be obtained by distillation with water. It is almost certainly *not* present in stinging nettles.

It is produced in the laboratory:

(1) By the oxidation of methyl alcohol and formaldehyde (Ber. **36,** 3304):

$$H\cdot CH_2OH \xrightarrow{O} H\cdot CHO \xrightarrow{O} H\cdot CO_2H.$$

(2) By heating hydrocyanic acid, the nitrile of formic acid, with alkalis or acids:

$$HCN + 2H_2O = HCOOH + NH_3.$$

(3) By boiling chloroform with alcoholic potassium hydroxide (*Dumas*):

$$CHCl_3 + 4KOH = HCOOK + 3KCl + 2H_2O.$$

(4) From chloral (Liebig), (5) from acetaldehyde disulphonic acid (see p. 247), and (6) from propargylic aldehyde (p. 255) and sodium hydroxide:

$$CCl_3\cdot CHO + NaOH = HCCl_3 + HCOONa;$$
$$(SO_3Na)_2CH\cdot CHO + NaOH = (SO_3Na)_2CH_2 + HCOONa;$$
$$CH{\equiv}C\cdot CHO + NaOH = CH{\equiv}CH + HCOONa.$$

(7) The direct production of formates by the action of CO on concentrated potassium hydroxide at 100°, or more easily on soda-lime at 200–220°, is of technical importance (*Berthelot*, Ann. **97,** 125: *Geuther*, Ann. **202,** 317: *Merz* and *Tibiriçá*, Ber. **13,** 718):

$$CO + NaOH = HCO\cdot ONa.$$

By working at high pressures the reaction proceeds at an appreciably lower temperature (D.R.P. 86419). The source of carbon monoxide on the large scale is "producer gas" obtained by incomplete combustion of coal.

Anhydrous formic acid is obtained from the formates prepared as above by treatment with sulphuric acid (C. 1905, I. 1701) or better, with sodium bisulphate (C. 1908, I. 998).

Similarly, ammonium formate is produced by passing a mixture of CO and NH_3 over heated catalysts (C. 1895, I. 367).

(8) By action of acids on *iso*cyanides or carbylamines (p. 293):

$$CN\cdot C_2H_5 + 2H_2O = HCO_2H + C_2H_5NH_2.$$

(9) From fulminic acid by means of concentrated hydrochloric acid (see formohydroxamic chloride, p. 289), hydroxylamine hydrochloride being formed simultaneously:

$$C:N\cdot OH + 2H_2O + HCl = H\cdot CO_2H + NH_2OH\cdot HCl.$$

(10) By the action of potassium on moist carbon dioxide (*Kolbe* and *Schmitt*, Ann. **119,** 251):

$$3CO_2 + 4K + H_2O = 2HCO\cdot OK + K_2CO_3.$$

Formates are also produced by the action of sodium amalgam or electrolytic hydrogen (Ber. **38,** 4138: **47,** 256, 541) on aqueous solutions of bicarbonates; likewise on boiling zinc carbonate with potassium hydroxide and zinc dust.

Potassium hydride combines at ordinary temperatures with CO_2, forming HCOOK. At higher temperatures (80°) there results a mixture of potassium formate and oxalate (C. 1905, II. 29). Potassium formate is also formed when CO and H_2 are passed together over heated potassium (*Moissan*, C. 1902, I. 568):

$$2CO + KH = HCO_2K + C.$$

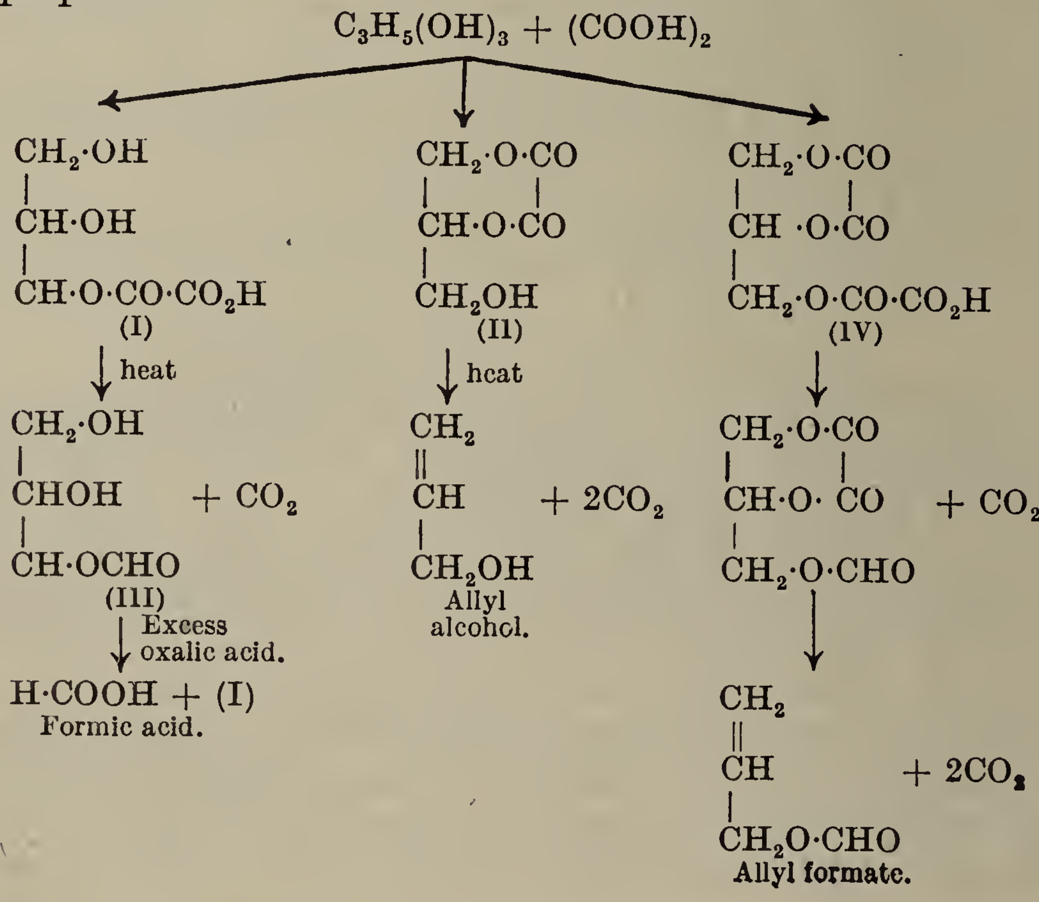
(11) *From Oxalic Acid.*—Before the development of the methods described under (7), formic acid was usually made by heating glycerol with oxalic acid, and this preparation is frequently now carried out as an exercise in the laboratory.

The mechanism of the reactions between glycerol and oxalic acid have been carefully investigated by Chattaway (J.C.S. **105,** 151 : **107,** 407) and can be conveniently dealt with here.

The first products formed from the glycerol and oxalic acid are, as would be expected, the acid oxalate (I) and normal oxalate (II) of glycerol. The existence of these esters in the reacting mixture is shown by the isolation of oxamic acid (from (I)) and oxamide (from (II)) by the action of ammonia, and oxanilic acid and oxanilide by the action of aniline.

The acid oxalate (I) breaks down on heating into glycerol monoformin (III), from which by the action of excess of oxalic acid, formic acid and more acid oxalate are produced. That this, rather than the traditional hydrolysis of the monoformin by water from the crystallized oxalic acid is the correct explanation is shown by the fact that formates yield formic acid by the action of *anhydrous* oxalic acid.

Similarly, the normal oxalate (II) breaks down on heating into allyl alcohol and CO_2. The presence of small quantities of allyl formate in allyl alcohol prepared by this method is due to the breakdown of the ester (IV) which is also formed in small amount. By the use of appropriate conditions, either formic acid or allyl alcohol can be prepared.

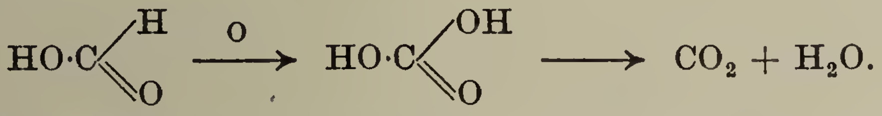


The acid prepared by this method is at first very dilute, but later the distillate contains 56% of formic acid. If anhydrous oxalic acid is employed from the beginning, formic acid of 95–98% content is obtained.

To obtain anhydrous formic acid from the aqueous solution, the acid is neutralized with lead oxide or lead carbonate and the lead formate decomposed at 100° with H_2S.

Properties.—Formic acid is a mobile liquid which possesses a pungent odour and causes blisters on the skin. It melts at $+ 8{\cdot}4°$ and boils at $100{\cdot}6°/760$ mm. $D_{20} = 1{\cdot}2199$. It mixes in all proportions with water, alcohol and ether, and yields the *hydrate* $4CH_2O_2 + 3H_2O$, which boils at 107·1°, with dissociation into formic acid and water. Concentrated hot sulphuric acid decomposes formic acid into carbon monoxide and water. A temperature of 160° suffices to break up the acid into carbon dioxide and hydrogen. The same change may occur at ordinary temperatures by the action of finely-divided rhodium, iridium, and ruthenium, but less readily when platinum sponge is employed.

The aldehydic nature of formic acid explains its reducing property, its ability to precipitate silver from a hot neutral solution of silver nitrate, and mercury from mercuric nitrate, being itself oxidized to carbon dioxide:



$$HO{\cdot}C\begin{matrix}/H\\ \backslash O\end{matrix} \xrightarrow{O} HO{\cdot}C\begin{matrix}/OH\\ \backslash O\end{matrix} \longrightarrow CO_2 + H_2O.$$

Formates, excepting the sparingly soluble lead and silver salts, are readily soluble in water. *Lead formate,* $(HCO_2)_2Pb$, crystallizes in beautiful needles and dissolves in 36 parts of cold water. *Silver formate,* HCO_2Ag, rapidly blackens on exposure to light.

Decomposition of Formates.—1. The alkali salts, heated to 250°, are converted into oxalates with evolution of hydrogen:

$$2HCO_2K = (CO_2K)_2 + H_2.$$

2. Potassium formate, when heated with an excess of potassium hydroxide, decomposes with the formation of carbonate and the liberation of pure hydrogen:

$$H{\cdot}CO_2K + KOH = K_2CO_3 + H_2.$$

3. The ammonium salt, heated to 230°, passes into formamide:

$$H{\cdot}CO_2NH_4 \xrightarrow[230°]{-H_2O} H{\cdot}CONH_2.$$

It may be distilled under reduced pressure without decomposition.

4. The silver salt and mercury salt, when heated, decompose into the metal, carbon dioxide and formic acid (C. 1905, II. 304):

$$2HCO_2Ag = 2Ag + CO_2 + H{\cdot}CO_2H.$$

5. The calcium salt, when heated with the calcium salts of higher fatty acids, yields aldehydes (p. 226).

6. Zinc formate and other formates undergo an intramolecular dismutation when heated at about 240° with formation of formaldehyde in good yield (Ber. **51**, 1398):

$$Zn(O{\cdot}CHO)_2 \longrightarrow ZnCO_3 + HCHO.$$

Esters of formic acid are prepared (1) from formic acid, alcohol, and hydrochloric or sulphuric acid; (2) from sodium formate and hydrochloric or sulphuric acid; (3) from a mixture of formyl acetic anhydride, or acetyl formyl oxide, $HCOOCOCH_3$, and alcohols (C. 1900, II. 314); (4) from glycerol, oxalic acid, and alcohol. They are agreeably-smelling liquids.

Methyl formate, m.p. $-100°$, b.p. 32·5° (Ber. **33**, 638).

Ethyl formate, b.p. 54·4°. This ester serves in the manufacture of artificial rum and arrack, and for the union of the formyl group with organic radicals (see Formyl acetone, etc.).

n-*Propyl ester*, b.p. 81°. n-*Butyl ester*, b.p. 107°. For higher esters consult Ann. **233**, 253; C. 1900, II. 314. *Allyl ester*, b.p. 90°.

Formamide, $HCO{\cdot}NH_2$, b.p. 192–195°, with partial decomposition, b.p. 90°/10 mm., is obtained (1) by heating ammonium formate (see above) to 230° (Ber. **12**, 973: **15**, 980), or (2) ethyl formate with alcoholic ammonia to 100°; (3) by boiling formic acid with ammonium thiocyanate (Ber. **16**, 2291). It consists of a thick liquid, miscible with water, alcohol, and ether. Heated rapidly it breaks down into CO and NH_3; P_2O_5 liberates hydrocyanic acid from it. It combines with chloral (p. 238) to form *chloral formamide*, $CCl_3{\cdot}CH(OH){\cdot}NHCHO$, m.p. 118°, which is employed as a narcotic under the name "*chloralamide.*"

Mercuric oxide dissolves in it with the formation of *mercury formamide*, $(CHO{\cdot}NH)_2Hg$. It is a feebly alkaline liquid, sometimes applied as a subcutaneous injection. For *sodium formamide*, see C. 1898, I. 927.

Formethylamide, $CHO{\cdot}NH{\cdot}C_2H_5$, b.p. 199°, is obtained from ethyl formate, also by distilling a mixture of ethylamine with chloral:

$$CCl_3{\cdot}CHO + NH_2{\cdot}C_2H_5 = CHO{\cdot}NH{\cdot}C_2H_5 + HCCl_3.$$

Formallylamide, b.p. 109°/15 mm. (Ber. **28**, 1666).

Formylhydrazine, $HCO{\cdot}NHNH_2$, m.p. 54°, is obtained from formic ester and hydrazine. It yields triazole (Ber. **27**, R. 801) when heated with formamide.

Diformylhydrazine, $HCONH{\cdot}NHCOH$, m.p. 106°, is obtained from an excess of formic ester and hydrazine, when heated to 130° (Ber. **28**, R. 242). Its lead salt with ethyl iodide yields *diformyldiethylhydrazine* (Ber. **27**, 2278).

Hydrocyanic acid, *hydrogen cyanide*, *prussic acid*, *formonitrile*, **HCN**, the nitrile of formic acid, was discovered by *Scheele* in 1782. *Gay-Lussac*, in 1811, obtained it anhydrous, in the course of his memorable investigations upon the radical cyanogen. In hydrogen cyanide he recognized the hydrogen derivative of a radical, consisting of carbon and nitrogen, for which he suggested the name *cyanogène* (*κύανος*, blue, *γεννάω*, to produce).

It occurs free in all parts of the Javanese tree, *Pangium edule*, Reinw. (Ber. **23**, 3548). It is obtained (1) from *amygdalin* (*q.v.*), a glucoside contained in bitter almonds, which, under favourable conditions, takes up water and breaks down into hydrocyanic acid, glucose, and benzaldehyde (*Liebig* and *Wöhler*, Ann. **22**, 1):

$$\underset{\text{Amygdalin.}}{C_{20}H_{27}NO_{11}} + 2H_2O \longrightarrow HCN + \underset{\text{Benzaldehyde.}}{C_6H_5CHO} + \underset{\text{Glucose.}}{2C_6H_{12}O_6}.$$

(2) By the action of phosphorus pentoxide on formamide:

$$H{\cdot}CONH_2 - H_2O \longrightarrow HCN.$$

(3) By the action of electric sparks on a mixture of acetylene and nitrogen (Berthelot) or by passing the mixture through an electric furnace (C. 1902, I. 525):

$$CH \vdots CH + N_2 \longrightarrow 2HCN.$$

(4) By the action of the silent electric discharge on a mixture of cyanogen and hydrogen:

$$(CN)_2 + H_2 \longrightarrow 2HCN.$$

(5) Ammonium cyanide is formed by heating chloroform with ammonia under pressure:

$$CHCl_3 + 5NH_3 \longrightarrow NH_4CN + 3NH_4Cl.$$

(6) By boiling formaldoxime with water:

$$CH_2 : NOH \xrightarrow{\hspace{2em}} HCN + H_2O.$$

(7) Hydrocyanic acid is prepared from metallic cyanides, usually potassium ferrocyanide, by the action of dilute sulphuric acid:

$$2K_4Fe(CN)_6 + 3H_2SO_4 = K_2Fe_2(CN)_6 + 3K_2SO_4 + 6HNC.$$

The aqueous acid thus obtained may be dehydrated by distillation over calcium chloride or phosphorus pentoxide.

Properties.—Anhydrous hydrogen cyanide is a mobile liquid, b.p. 26·5°, m.p. $-15°$, $D_{18} = 0·697$. It is an endothermic compound with a heat of formation $-27·5$ Cals. per Mol., and under strong excitation can be caused to detonate.

It possesses a peculiar odour resembling that of oil of bitter almonds, and is extremely poisonous.

It is a feeble acid, imparting a faint red colour to blue litmus. Carbon dioxide decomposes its alkali salts. Like the halogen acids, it reacts with metallic oxides, producing cyanides. From solutions of silver nitrate it precipitates silver cyanide, a white, curdy precipitate.

Reactions.—(1) The aqueous acid decomposes readily on standing, yielding ammonium formate and brown substances. The presence of a very slight quantity of stronger acid renders it more stable. When warmed with mineral acids it breaks up into formic acid and ammonia:

$$HNC + 2H_2O = HCOOH + NH_3.$$

(2) Dry hydrocyanic acid combines directly with the gaseous halogen acids to form crystalline compounds (p. 289) (J.C.S. **1930,** 1834). The acid also unites with some metallic chlorides, *e.g.* Fe_2Cl_6, $SbCl_5$.

(3) Nascent hydrogen (zinc and hydrochloric acid) reduces it to methylamine (p. 196).

(4) Hydrocyanic acid unites with aldehydes and ketones to form *cyanohydrins*, the nitriles of α-hydroxy-acids. This rather important synthesis is especially interesting for the building up of the aldoses.

(5) Hydrocyanic acid, or potassium cyanide, unites with many αβ-unsaturated carboxylic acids and αβ-olefine ketones, producing thereby saturated nitrilo-carboxylic acids and nitrilo-ketones (Ann. **293,** 338: Ber. **37,** 4065: C. 1905, I. 171).

(6) When hydrocyanic acid and hydrogen chloride react with many phenolic compounds in presence of anhydrous aluminium chloride, the aldimines of hydroxyaldehydes are formed and can be readily hydrolysed to the aldehyde (*Gatterman*: see also Vol. II):

$$C_6H_5OH + HCN + [HCl] \xrightarrow{\hspace{2em}} C_6H_4(OH)\cdot CH : NH + [HCl].$$

(7) Formimido ethers, $NH : CH(OR)$ (p. 288), are obtained in the form of their hydrochlorides by the action of HCl on a mixture of an alcohol and anhydrous HCN: formamidoxime, $H\cdot C(: NOH)NH_2$ (p. 289), is formed when an alcoholic solution of hydrocyanic acid and hydroxylamine is evaporated to dryness.

Constitution of Hydrocyanic Acid.—Two formulæ have to be considered for hydrocyanic acid, for each of which a number of reactions afford support:

(1) $H\cdot C \vdots N$, in which the compound is represented as the nitrile of formic acid (nitrile formula).

(2) H·N : C, in which the compound is represented as the imine of carbon monoxide (*iso*nitrile formula).

The first formula is supported by the formation from formamide and by the formation of ammonium formate on hydrolysis, and by the fact that methylation by diazomethane leads chiefly to the production of acetonitrile, $CH_3 \cdot C \vdots N$. On the other hand, a series of addition reactions with halogens, oxygen, sulphur agree better with the second formula, which was put forward by Nef. The high toxicity of hydrogen cyanide is also in keeping with the *iso*nitrile formula.

The use of physical methods has not succeeded in solving the constitution. The evidence so far supports the existence of an equilibrium : $H \cdot CN \rightleftarrows H \cdot NC$ in free hydrocyanic acid, the equilibrium at ordinary temperatures being chiefly in the direction of the left-hand side, only traces of the *iso*nitrile being present under these conditions (J.C.S. **121**, 1604 : see also J.C.S. **1928**, 540 : discussion on the present knowledge of the subject, see Ber. **54**, 1709).

Polymerization of Hydrocyanic Acid.—When the aqueous acid stands for some time in contact with alkali hydroxides, or with alkali carbonates, or if the anhydrous acid be mixed with a small piece of potassium cyanide, not only brown substances separate, but also white crystals, soluble in ether, and having the same percentage composition as hydrocyanic acid. Inasmuch as they break down, on boiling, into glycocoll, $NH_2 \cdot CH_2CO_2H$, carbon dioxide and ammonia, they are assumed to be the *nitrile* of *aminomalonic acid*, $(CN)_2CHNH_2$ (Ber. **7**, 767). They decompose at 180°, with explosion and partial re-formation of hydrocyanic acid.

Detection.—To detect small quantities of free hydrocyanic acid or its soluble salts, the solution under examination is saturated with potassium hydroxide, a solution of a ferrous salt, containing some ferric salt is added, and the mixture is boiled for a short time. Hydrochloric acid is added to dissolve the precipitated iron oxides ; if any insoluble Prussian blue should remain, it would indicate the presence of hydrocyanic acid. The following reaction is more sensitive. A few drops of yellow ammonium sulphide are added to the hydrocyanic acid solution, and this then evaporated to dryness. Ammonium thiocyanate will remain, and if added to a ferric salt, will colour it a deep red.

Salts of Hydrocyanic Acid.—*Cyanides and Double Cyanides.*—The importance of the cyanides and double cyanides in analytical chemistry explains the reason for the discussion of hydrocyanic acid and its salts in inorganic text-books. In organic chemistry the metallic cyanides serve for the introduction of the *cyanogen group* into carbon compounds (comp. acid nitriles, α-ketone acids, etc.).

The alkali cyanides may be formed by the direct action of these metals on cyanogen gas ; thus, potassium burns with a red flame in cyanogen, at the same time yielding potassium cyanide, $C_2N_2 + K_2 = 2KNC$. They are also produced when nitrogenous organic substances are heated together with alkali metals. The strongly basic metals dissolve in hydrocyanic acid, forming cyanides. A more common procedure is to act with the acid on metallic oxides and hydroxides :

$$HNC + KOH = KNC + H_2O ; \quad 2HNC + HgO = Hg(CN)_2 + H_2O.$$

The insoluble cyanides of the heavy metals are obtained by the double decomposition of the metallic salts with potassium cyanide.

The cyanides of the light metals, especially the alkali and alkali earths, are easily soluble in water, react alkaline, and are decomposed by acids, even carbon dioxide, with elimination of hydrogen cyanide; yet they are very stable and undergo no change even at a red heat. The cyanides of the heavy metals, however, are mostly insoluble, and are only decomposed by strong acids. When ignited, the cyanides of the noble metals undergo decomposition, breaking up into cyanogen gas and metals.

The following simple cyanides are especially important in organic chemistry:

Alkali Cyanides.—Sodium cyanide is manufactured by the action of carbon on sodamide (Castner's process). The reaction takes place in two stages:

(1) At 400°. $2NaNH_2 + C \longrightarrow 2H_2 + \underset{\text{(Sodium cyanamide.)}}{Na{\cdot}N:C:N{\cdot}Na}$.

(2) At 600°. $Na{\cdot}N:C:N{\cdot}Na + C \longrightarrow 2NaCN$.

Various other methods are used for the preparation of sodium and potassium cyanides, which are described in text-books of Inorganic Chemistry.

Reactions of the Alkali Cyanides.—Their aqueous or alcoholic solutions become brown on exposure to the air, and decompose, more rapidly on boiling, into formates and ammonia. When fused in the air, as well as with easily reducible metallic oxides, the salts take up oxygen and are converted into cyanates (*q.v.*). On being melted with sulphur they form thiocyanates (*q.v.*). When the alkyl halides or salts of alkylsulphuric acids are heated with potassium cyanide, acid nitriles with varying amounts of isomeric carbylamines, or *iso*nitriles are produced. Many organic halogen substitution products are converted into nitriles through the agency of potassium cyanide. Ethyl hypochlorite and potassium cyanide yield chlorimidocarbonic ester (Ann. **287**, 274).

Ammonium cyanide, NH_4NC, is formed by the direct union of HNC with ammonia, by heating carbon in ammonia gas; by the action of ammonia on chloroform (p. 290); by the action of the silent electric discharge on methane and nitrogen; and by conducting carbon monoxide and ammonia through red-hot tubes. It is best prepared by subliming a mixture of potassium cyanide or dry ferrocyanide with ammonium chloride. It consists of colourless cubes, easily soluble in alcohol, and subliming at 40°, with partial decomposition into NH_3 and HNC. When preserved it becomes dark in colour and decomposes. It unites with aldehydes and ketones with the elimination of water to form α-aminonitriles, *e.g.* with formaldehyde it forms methyleneaminoacetonitrile, $CH_2:N{\cdot}CH_2{\cdot}CN$.

Mercuric cyanide, $Hg(CN)_2$, is obtained by dissolving mercuric oxide in hydrocyanic acid, or by boiling Prussian blue (8 parts) and mercuric oxide (1 part) with water until the blue coloration disappears. It dissolves readily in hot water (in 8 parts cold water), and crystallizes in bright, shining, quadratic prisms. When heated it yields cyanogen and mercury. It forms acetyl cyanide, $CH_3{\cdot}CO{\cdot}CN$, with acetyl chloride.

Silver cyanide, AgNC, combines with alkyl iodides to yield addition products, which pass into *iso*nitriles when they are heated (p. 293; C. 1903, II. 827).

The chief use of potassium cyanide is in the preparation of acid nitriles of various kinds, by reaction with alkyl halides, alkyl sulphates, and halogen substitution products of the fatty acids. In many instances mercury cyanide or silver cyanide is preferable, *e.g.* in the formation of α-ketonic nitriles from acid chlorides or bromides. It is interesting to note that by the interaction of alkyl iodides and silver cyanide iso*nitriles* or *carbylamines* are formed; in them the alcohol radical is joined to nitrogen.

Compound Metallic Cyanides.—The cyanides of the heavy metals, insoluble in water, dissolve in aqueous potassium cyanide, forming crystallizable double cyanides, which are soluble in water. Most of these compounds behave like double salts. Acids decompose them in the cold, with liberation of hydrocyanic acid and the precipitation of the insoluble cyanides:

$$AgCN{\cdot}KCN + HNO_3 = AgCN + KNO_3 + HNC.$$

In others, however, the metal is in more intimate union with the cyanogen group, and the metals in these cannot be detected by the usual reagents. Iron, cobalt, platinum, also chromium and manganese in their most highly oxidized state, form cyanogen derivatives of this class. The stronger acids do not eliminate hydrocyanic acid from them, even in the cold, but the corresponding acids are set free, and these are capable of producing salts:

$$K_4Fe(CN)_6 + 4HCl = H_4Fe(CN)_6 + 4KCl.$$

The most important compound metallic cyanides, particularly potassium ferrocyanide or yellow prussiate of potash, and potassium ferricyanide or red prussiate of potash, are described in inorganic text-books.

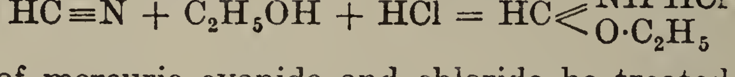
Hydroferrocyanic acid, $H_4Fe(CN)_6$, is precipitated by ether, from its solution in alcohol, as a pure white compound with ether (C. 1900, II. 1151). This is decomposed at 90° *in vacuo.* It is assumed that the union with ether occurs at the oxygen atom, which behaves as a tetravalent atom (comp. p. 156: Ber. **34**, 3612: **35**, 93): esterification of $H_4Fe(CN)_6$, see Monatsh. **48**, 71.

Sodium Nitroprusside, $Fe(CN)_5(NO)Na_2 + 2H_2O$.—Hydronitroprussic acid is formed when nitric acid acts on potassium ferrocyanide (C. 1897, I. 909). The filtrate from the potassium nitrate is neutralized with sodium carbonate, and yields the sodium salt in beautiful red rhombic prisms, easily soluble in water.

It serves as a very delicate reagent for alkali sulphides and hydrogen sulphide, with which it gives an intense violet coloration.

Formimido-ethers, formhydroxamic acid, formyl chloridoxime, methyl nitrolic acid, formamidine, thioformethylimide, and *formamidoxime* are intimately related to hydrocyanic acid and formamide. They are representatives of groups of bodies which will be discussed in connection with acetic acid and its homologues.

The **formimido-ethers,** such as $HC{<}^{OC_2H_5}_{NH}$, are only known in the form of hydrochlorides. They are obtained from hydrocyanic acid, alcohol and HCl (Ber. **16**, 354, 1644):



$$HC{\equiv}N + C_2H_5OH + HCl = HC{<}^{NH{\cdot}HCl}_{O{\cdot}C_2H_5}$$

If a mixture of mercuric cyanide and chloride be treated with HCl gas in alcohol-ether solution, a double salt results, $[HC(OC_2H_5):NH]HCl{\cdot}HgCl_2$ (C. 1904, I. 1064).

Upon standing in contact with alcohols they pass into esters of orthoformic acid (*q.v.*). They yield amidines with ammonia and amines (primary and secondary).

Thioformethylimide, $HC{<}\genfrac{}{}{0pt}{}{SH}{NC_2H_5}$, b.p. 125°/14 mm., is produced by the union of ethyl *iso*cyanide, in alcoholic solution, with hydrogen sulphide. It is a yellow oil (Ann. **280**, 297).

Thioformic acid, $HCO{\cdot}SH$, is obtained as its sodium salt when formic phenyl ester (Vol. II) is hydrolysed with alcoholic NaSH. The free acid is a very unstable liquid, which quickly polymerizes (C. 1905, I. 20).

Formamidine, $HC{<}\genfrac{}{}{0pt}{}{NH_2}{NH}$, is only known in the form of salts. Its hydrochloride is obtained (1) by the action of ammonia on formimidoethyl ether hydrochloride (Ber. **16**, 375, 1647):

$$HC{<}\genfrac{}{}{0pt}{}{OC_2H_5}{NH{\cdot}HCl} + NH_3 = HC{<}\genfrac{}{}{0pt}{}{NH_2{\cdot}HCl}{NH} + HOC_2H_5.$$

(2) from formimide chloride, the addition product of hydrochloric acid and hydrocyanic acid, when it is digested with alcohol:

$$2HC{<}\genfrac{}{}{0pt}{}{Cl}{NH} + 2C_2H_5OH = HC{<}\genfrac{}{}{0pt}{}{NH_2{\cdot}HCl}{NH} + C_2H_5Cl + HCO_2C_2H_5.$$

Formhydroxamic acid, $HC{<}\genfrac{}{}{0pt}{}{NOH}{OH}$, m.p. 80°, is produced when equimolecular quantities of formic ester and hydroxylamine are allowed to stand in a solution of absolute alcohol; also, by the oxidation of methylamine with persulphuric acid (comp. p. 196) (Ber. **35**, 4299). It forms brilliant leaflets, which dissolve readily in water and in alcohol, but sparingly in ether. At temperatures above its melting-point violent decomposition takes place, a change which occurs slowly and completely at ordinary temperatures. The acid yields an intense red coloration with ferric chloride. It reduces Fehling's solution, and its mercury salt in dry condition explodes when it is rubbed; copper salt, $HCNO_2Cu$ (comp. Ber. **33**, 1975). It has been suggested as the first stage in the photosynthesis of amino-acids (J.C.S. **121**, 1078).

Formyl chloridoxime, *Formoximinochloride,* $HC{<}\genfrac{}{}{0pt}{}{NOH}{Cl}$, is a beautifully crystalline, very easily decomposed compound, with a sharp, penetrating odour. It is produced when fulminates (p. 294) are treated, in the cold, with concentrated hydrochloric acid. It dissolves in ether. When its solution is warmed with concentrated hydrochloric acid, it rapidly decomposes into formic acid and hydroxylamine hydrochloride:

$$HC{<}\genfrac{}{}{0pt}{}{NOH}{Cl} + 2H_2O = H{\cdot}C{<}\genfrac{}{}{0pt}{}{O}{OH} + NH_2OH{\cdot}HCl.$$

In aqueous solution the compound readily reverts to fulminates. Silver nitrate changes it to silver fulminate and silver chloride. Aniline converts it into phenyl *iso*uretine (Vol. II), and with ammonia it yields cyano*iso*nitrosoacethydroxamic acid, a derivative of mesoxalic acid (Ann. **280**, 303).

Acetyl formyl chloride oxime is obtained from the product of reaction between acetic anhydride, formhydroxamic acid and PCl_5. Silver nitrate converts it into silver fulminate, silver chloride, and acetic acid (Ann. **310**, 19: Ber. **38**, 3858).

Formonitroxime, *Methylnitrolic acid,* $HC{<}\genfrac{}{}{0pt}{}{NO_2}{NOH}$, is prepared from: (1) nitromethane (p. 180) and nitrous acid, and (2) *iso*nitrosoacetic acid (p. 460) and N_2O_4. It is decomposed by boiling with water or dilute acids into N_2O and formic acid, and into HNO_2 and fulminic acid (p. 294) (Ber. **40**, 418).

Formamidoxime, iso*Uretin,* $HC{<}\genfrac{}{}{0pt}{}{NH_2}{N(OH)}$, m.p. 114°, is isomeric with urea, $CO(NH_2)_2$. It results from the evaporation of an alcoholic solution of hydroxylamine and hydrogen cyanide (*Lossen* and *Schifferdecker*, Ann. **166**, 295).

*Methyl*iso*uretin*, $NH_2CH : NOCH_3$, m.p. 40°, is prepared from *iso*uretin, alkali hydroxide, and iodomethane (Ann. **310**, 2).

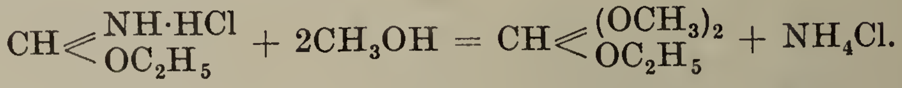
Formazyl hydride, $HC{<}\genfrac{}{}{0pt}{}{N{=}N{\cdot}C_6H_5}{N{-}NH{\cdot}C_6H_5}$, m.p. 119–120°, is obtained from formazyl carboxylic acid (see p. 542).

Derivatives of Orthoformic acid.

Orthoformic esters are formed (1) when chloroform is heated with sodium alcoholates in alcoholic solution (*Williamson* and *Kay*, Ann. **92**, 346):

$$CHCl_3 + 3CH_3{\cdot}ONa = CH(OCH_3)_3 + 3NaCl\,;$$

(2) when formimido-ethers (p. 288) react with alcohols, mixed esters being also produced (*Pinner*, Ber. **16**, 1645):



$$CH{<}^{NH{\cdot}HCl}_{OC_2H_5} + 2CH_3OH = CH{<}^{(OCH_3)_2}_{OC_2H_5} + NH_4Cl.$$

They are converted by alcoholic alkali hydroxides into alkali formates, and by glacial acetic acid into acetic esters and ordinary formic esters. Orthoformic ester changes ketones and aldehydes into ortho-ethers, *e.g.* $(CH_3)_2C(OC_2H_5)_2$ (p. 266), and acetal, $CH_3{\cdot}CH(OC_2H_5)_2$ (p. 241), and at the same time, is converted into ordinary formic ester (Ber. **29**, 1007). Orthoformic ester, in the presence of acetic anhydride and aided by heat, combines with acetyl acetone, acetoacetic ester and malonic ester to yield ethoxymethylene derivatives (Ber. **26**, 2729).

Methyl orthoformate, $CH(OCH_3)_3$, b.p. 102°. *Ethyl ester*, $CH(OC_2H_5)_3$, b.p. 146°. *Allyl ester*, $CH(OC_3H_5)_3$, b.p. 196–205° (Ber. **12**, 115).

Orthothioformic ester, $CH(SC_2H_5)_3$, b.p. 116°/10 mm., is prepared from formic acid ester, or amide, by the action of ethyl mercaptan and hydrochloric acid; also from chloroform and sodium mercaptide. It is a colourless oil of unpleasant odour. It is very stable towards alkalis, but is hydrolysed by acids. Permanganate decomposes it into ethanesulphonic acid and methylene diethyl sulphone (Ber. **40**, 740).

Chloroform, *Trichloromethane*, $CHCl_3$, m.p. − 62° (Ber. **26, 1053**), b.p. 61·5°, $D_{15} = 1{\cdot}5008$, is obtained: (1) by the chlorination of CH_4 or CH_3Cl; (2) by the action of bleaching powder on different carbon compounds—*e.g.* ethyl alcohol, acetone, etc.; (3) by heating chloral (p. 238) and other aliphatic bodies having a terminal CCl_3-group—*e.g.* trichloroacetic acid and trichlorophenomalic acid (*q.v.*)—with aqueous potassium or sodium hydroxide:

$$\underset{\text{Chloral.}}{CCl_3{\cdot}CHO} + KOH = CHCl_3 + \underset{\text{Potassium formate.}}{HCO_2K.}$$

Chloroform is prepared technically by treating alcohol and acetone with bleaching powder which acts both as an oxidizing and chlorinating substance. The resulting $CCl_3{\cdot}CHO$ or $CH_3{\cdot}CO{\cdot}CCl_3$ is decomposed by lime (Mechanism of the Reaction: *Zincke*, Ber. **26**, 501, note). Pure chloroform can be obtained by decomposing pure chloral with potassium hydroxide; or by freezing out crystals of chloroform and centrifugation (*R. Pictet*). Perfectly pure chloroform results in the decomposition of salicylide-chloroform (*Anschütz*, Ann. **273**, 73).

Historical.—Chloroform was discovered in 1831 by *Liebig* and *Soubeiran*. It was not until 1835 that *Dumas* proved conclusively that it contained hydrogen. In 1847 *Simpson*, of Edinburgh, introduced chloroform into surgery.

Properties.—Chloroform is a colourless liquid of an agreeable ethereal odour and sweetish taste. It is an excellent solvent for iodine and many organic substances, some of which crystallize out with "chloroform of crystallization," *e.g.* salicylide-chloroform (see above). Chloroform seems to enter into a loose combination with ether, which is evidenced by a rise of temperature when the two liquids are mixed. Inhalation of its vapours produces anæsthesia. It is uninflammable. It forms C_6Cl_6 when it is conducted through tubes heated to redness.

Reactions.—(1) Chloroform is oxidized by the prolonged action of sunlight in presence of the oxygen of the air to phosgene (C. 1905, II. 1623). To prevent this about one per cent. of alcohol is added. Chromic acid also converts chloroform into this phosgene.

(2) Chlorine converts chloroform into CCl_4.

(3) When heated with aqueous or alcoholic potassium hydroxide it forms potassium formate (p. 283) and carbon monoxide. The latter is probably a product of reaction with the $:CCl_2$ group, which is formed by the expulsion of HCl from the chloroform by the action of the alkali. It then unites with the alkali, whereby the more formic acid is produced the higher the temperature of reaction (Ann. **302**, 274):

$$CHCl_3 + 4KOH = HCOOK + 3KCl + 2H_2O.$$

(4) Orthoformic acid ester, $CH(O\cdot C_2H_5)_3$, is produced when chloroform is treated with sodium alcoholate.

(5) When heated to 180° with alcoholic ammonia, it forms ammonium cyanide and chloride. When potassium hydroxide is present, an energetic reaction takes place at ordinary temperatures as follows:

$$CHCl_3 + NH_3 + 4KOH = KNC + 3KCl + 4H_2O.$$

(6) *iso*Nitriles (p. 293), having extremely disgusting odours, are formed when chloroform is heated with primary bases and potassium hydroxide. This reaction serves both for the detection of chloroform and also of the primary amines. (*Carbylamine reaction.*)

(7) Chloroform yields an additive product with acetone, trichloro-*tert.*-butyl alcohol.

(8) It is converted by sodium acetoacetic ester into *m*-hydroxyuvitic acid (Vol. II).

(9) Aromatic hydroxyaldehydes are produced when chloroform is digested with phenols and sodium hydroxide (*Reiner-Tiemann reaction*, see Vol. II), *e.g.*:

$$\underset{\text{Phenol.}}{C_6H_5OH} + CHCl_3 + 4KOH \longrightarrow \underset{\text{Salicylaldehyde.}}{C_6H_4(OH)\cdot CHO} + 3KCl + 3H_2O.$$

Bromoform, $CHBr_3$, m.p. 7·8°, b.p. 151°, $D_{15} = 2\cdot 9$, is produced by the action of bromine and KOH or lime (*Löwig*, 1832) on alcohol or acetone; by electrolysis of a solution of acetone and potassium bromide (C. 1902, I. 455: 1904, II. 301); from chloroform and aluminium bromide (C. 1900, I. 1201: 1901, I. 666); and also from tribromopyroracemic acid (*q.v.*).

Iodoform, CHI_3, m.p. 120°, is formed when iodine and potassium hydroxide act on ethyl alcohol, acetone, aldehyde and other substances containing the group $CH_3\cdot C\begin{smallmatrix}/\\ -O-\\ \backslash\end{smallmatrix}$ Pure methyl alcohol does not yield iodoform (Ber. **13**, 1002).

The formation of tri-iodoaldehyde and tri-iodoacetone precedes the production of the iodoform. These substances are very unstable in the presence of alkalis. When tri-iodoacetic acid is warmed with acetic acid, or when it is treated with alkali carbonates, it breaks down into iodoform and carbon dioxide. Iodoform can be obtained by electrolysis of an aqueous solution of KI, Na_2CO_3 and alcohol, or KI and acetone (C. 1897, II. 695: 1898, I. 31: 1900, II. 19: 1904, I. 995). Acetylene-mercury chloride, $C_2H_2\cdot HgCl_2$, also yields iodoform when acted on by iodine and alkali (C. 1902, II. 1499).

Iodoform crystallizes in brilliant, yellow leaflets, or hexagonal plates (C. 1899, I. 189: 1901, II. 23), soluble in alcohol and ether, but insoluble in water. Its odour is saffron-like. It evaporates at medium temperatures and distils in steam. Digested with alcoholic KOH, HI, or potassium arsenite, it passes into methylene iodide (p. 243). Light and air decompose iodoform into CO_2, CO, I, and water (C. 1905, II. 1718).

Historical.—Iodoform was discovered in 1832 by *Serullas*. *Dumas*, in 1834, proved that it contained hydrogen, and in 1880 it was applied by *Mosetig-Moorhof* in Vienna in the treatment of wounds.

Fluoroform, CHF_3, is obtained from silver fluoride and chloroform, or better, iodoform mixed with sand. It is a gas (Ber. **23**, R. 377, 680 : C. 1900, I. 886). **Fluorochloroform,** $CHCl_2F$., b.p. 14·5° ; **fluorochlorobromoform,** **CHClFBr,** b.p. 38° (Ber. **26**, R. 781).

Nitroform, $CH(NO_2)_3$, has been described already, in connection with the nitroparaffins (p. 186).

Methanetrisulphonic acid, *formyltrisulphonic acid,* $CH(SO_3H)_3$, is produced by the action of sodium sulphite on chloropicrin, $CCl_3(NO_2)$ (*q.v.*), and when fuming sulphuric acid acts on calcium methane sulphonate (p. 176). The acid is very stable, even in the presence of boiling alkalis (C. 1899, I. 182).

In this connection may be mentioned also dibromonitromethane (p. 182), nitromethane disulphonic acid (Ann. **161**, 161), and hydroxymethane disulphonic acid, $CH(OH)(SO_3H)_2$ (Ber. **6**, 1032) ; dichloromethane monosulphonic acid, dichloromethyl alcohol (known only as acetic ester).

CARBON MONOXIDE, *iso*NITRILES AND FULMINIC ACID

Carbon monoxide, CO, m.p. − 211°, b.p. − 190°/760 mm., critical temperature — 141°, critical pressure 35 atmospheres, a colourless, combustible gas, the product of the incomplete combustion of carbon, is discussed in inorganic text-books. The methods for its production and its reactions, which are of importance in organic chemistry, will again be briefly reviewed. Carbon monoxide is obtained (1) from formic acid, oxalic acid, α-ketonic acids such as pyroracemic acid and benzoyl formic acids (Vol. II) ; (2) from α-hydroxy-acids such as glycollic acid, lactic acid, malic acid, citric acid, and mandelic acid (Vol. II) ; (3) from tertiary carboxylic acids of the formula $R_3C{\cdot}COOH$, such as trimethylacetic acid (p. 305), triphenylacetic acid (Vol. II), camphoric acid, cineolic acid (Vol. II), by the action of concentrated or fuming sulphuric acid (comp. Ber. **39**, 51). It is also made from hydrocyanic acid if, in preparing the latter from potassium ferrocyanide, $K_4Fe(CN)_6{\cdot}3H_2O$, concentrated sulphuric acid be substituted for the more dilute acid ; in this manner the hydrocyanic acid is changed to formamide, and the latter immediately breaks down into ammonia and carbon monoxide. Formamide yields carbon monoxide on the application of heat.

Reactions.—(1) Carbon monoxide and hydrogen exposed to the influence of electric discharges yield *methane* (p. 92). Being an unsaturated compound, carbon monoxide unites (2) with oxygen, giving a feebly luminous but beautifully blue flame, forming *carbon dioxide* ; (3) with sulphur yielding *carbon oxysulphide* ; and (4) with chlorine, to form *carbon oxychloride* or phosgene. It also combines directly with certain metals. (5) With potassium it forms the potassium derivative of *hexahydroxybenzene*, $C_6(OK)_6$ (see Vol. II). (6) Carbon monoxide is absorbed by sodium alkyls with the formation of dialkyl ketones, tertiary alcohols and other products (Ber. **52**, 1910). (7) With nickel it yields *nickel carbonyl*, $Ni(CO)_4$, b.p. 43° (*Mond*, *Quincke*, and *Langer*, Ber. **23**, R. 628 : C. 1903, I. 1250 : 1904, II. 1111) ; (8) With iron it yields *iron carbonyl*, $Fe(CO)_5$, b.p. 102° (C. 1906, I. 333 : 1907, I. 1179). It forms (9) *alkali formates* with the alkali hydroxides (p. 282), and (10) with sodium methoxide and sodium ethoxide it yields sodium acetate and propionate.

The "acetal" corresponding to carbon monoxide, **diethoxymethylene**, $C(OEt)_2$, b.p. 77°/760 mm., is obtained from ethyl formate by the following series of reactions:

$$H{\cdot}CO_2Et \xrightarrow{NaOEt} C(ONa)(OEt) \xrightarrow{POCl_3} CCl(OEt) \xrightarrow{NaOEt} C(OEt)_2.$$

It is a colourless liquid, broken down by acids into carbon monoxide and two mols. of alcohol (Ber. **60**, 554).

Carbon monosulphide, CS, is not known (Ber. **28**, R. 388).

The *iso***cyanides** (*isonitriles*, *carbylamines*) are isomeric with the nitriles or alkyl cyanides, but differ from them in having the alkyl group linked to nitrogen:

R·CN	R·NC
Nitrile.	*iso*Cyanide.

They were first prepared by Gautier (Ann. **151**, 239). The first step is the action of an alkyl iodide (1 mol.) on silver cyanide (2 mols.), the second step the decomposition of the addition compound between the *iso*nitrile and the silver cyanide by distillation with potassium cyanide.

1*a*. $C_2H_5I + 2AgCN = C_2H_5NC{\cdot}AgCN + AgI$

1*b*. $C_2H_5NC{\cdot}AgCN + KCN = C_2H_5NC + AgCN{\cdot}KCN$.

Shortly afterwards, *A. W. Hofmann* (Ann. **146**, 107) found that *iso*nitriles were produced by digesting chloroform and primary amines with alcoholic potassium hydroxide:

2. $C_2H_5NH_2 + CHCl_3 + 3KOH = C_2H_5NC + 3KCl + 3H_2O$.

3. The *iso*nitriles are produced as by-products in the preparation of the nitriles from alkyl iodides or sulphates and potassium cyanide.

Properties.—The carbylamines are colourless liquids which can be distilled, and possess an exceedingly disgusting odour. They are sparingly soluble in water, but readily soluble in alcohol and ether.

Reactions.—(1) The *iso*nitriles are characterized by their decomposition by dilute acids into formic acid and primary amines. This reaction proceeds readily by the action of dilute acids (HCl), or by heating with water to 180°:

$$C_2H_5{\cdot}NC + 2H_2O = C_2H_5NH_2 + HCO_2H.$$

(2) With fatty acids the *iso*nitriles yield fatty acid alkylamides.

(3) The *iso*nitriles, like hydrocyanic acid (p. 285), form crystalline derivatives with HCl; these are probably the hydrochlorides of alkyl formimide chlorides, $2CH_3NC{\cdot}3HCl = [CH_3N:CHCl]_2HCl$, which water decomposes into formic acid and amino- bases.

(4) Mercuric oxide changes the *iso*nitriles into *iso*cyanic esters, $C_2H_5N{=}CO$, with the separation of mercury, while P_2S_5 produces *iso*thiocyanates.

(5) Heat converts the *iso*nitriles into the normal nitriles, RC ⋮ N, with intermediate polymerization products (C. 1907, I. 948).

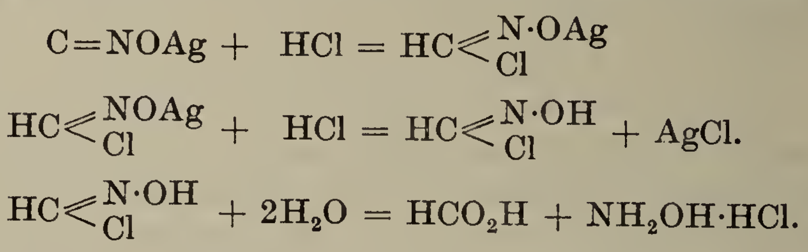
(6) Alkyl iodides and metallic cyanides unite with the *iso*nitriles to form double compounds (see above); RNC·CNAg can be looked on as being an ester of a hydrosilvercyanic acid, $HAg(CN)_2$ (C. 1903, II. 827: 1907, I. 948).

Methyl *iso***cyanide,** *Methyl carbylamine*, CH_3NC, b.p. 59°. **Ethyl** *iso***cyanide,** *Ethyl carbylamine*, C_2H_5NC, b.p. 79°, when heated at from 230° to 250°, undergoes atomic rearrangement into propionitrile. It combines with chlorine to yield ethylimidocarbonyl chloride, a derivative of carbonic acid; similarly, with bromine to form ethyl carbylamine bromide (C. 1904, II. 29). With H_2S it forms thioformethylimide (p. 289) and with acetyl chloride it produces ethylimidopyruvyl chloride, a derivative of pyroracemic acid (Ann. **280**, 291). *n*-**Propyl** *iso***cyanide**, b.p. 98°. *n*-**Butyl** *iso***cyanide**, b.p. 119° (C. 1900, II. 366).

Structure of the iso*Nitriles.*—From the hydrolysis of the *iso*nitriles to formic acid and a primary amine, as opposed to the hydrolysis of the nitriles to a fatty acid and ammonia, it is evident that the alkyl group in the *iso*nitriles must be linked to nitrogen. The original formula given to these compounds was $R{\cdot}N \vdots C$, but Nef (Ann. **270**, 267) suggested in 1892 that the properties of the compounds were better represented by the formula $R{\cdot}N : C$, which is in accord with the fact that in all addition reactions in which these compounds take part, the addition takes place entirely to the carbon atom and not to the C : N linking. A more recent formula, showing the compounds as containing a co-ordinate link, was suggested by Langmuir (J.A.C.S. **41**, 1543), and Sidgwick and others (J.C.S. **1930**, 1876) have obtained definite evidence in favour of Langmuir's formula by measurements of the parachors and dipole moments of the *iso*cyanides.

The compounds can therefore be best represented by the formula containing a co-ordinate link, $R{-}N\overset{\rightarrow}{=}C$.

Fulminic acid, (*Carbyloxime*), C : NOH,* is the oxime corresponding to carbon monoxide, and possesses the properties of a strong acid (*R. Scholl*, Ber. **23**, 3506: *Nef*, Ann. **280**, 303; comp. also, Ber. **27**, 2817). The fulminates have the same percentage composition as the salts of cyanic acid, and constitute one of the first examples of isomeric compounds (*Liebig*, 1823). Little is known about the free acid. Its odour is very similar to that of hydrocyanic acid, and is as poisonous. The acid is formed when the fulminates are decomposed by strong acids. It combines quite readily with the latter,—*e.g.* it yields formyl chloridoxime with hydrochloric acid (p. 289), which breaks down very easily with the formation of fulminic acid. The reaction of the fulminates with hydrochloric acid affords some insight into the constitution of fulminic acid itself. First, hydrochloric acid unites directly and salts of formyl chloridoxime arise, from which, by the absorption of water, formic acid and hydroxylamine are formed:

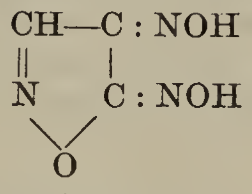


$$C{=}NOAg + HCl = HC{<}\begin{smallmatrix}N{\cdot}OAg\\ Cl\end{smallmatrix}$$

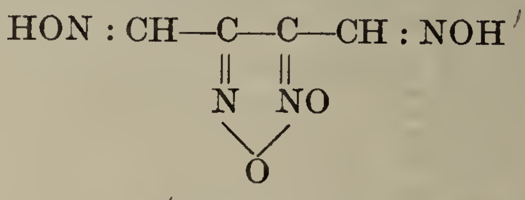
$$HC{<}\begin{smallmatrix}NOAg\\ Cl\end{smallmatrix} + HCl = HC{<}\begin{smallmatrix}N{\cdot}OH\\ Cl\end{smallmatrix} + AgCl.$$

$$HC{<}\begin{smallmatrix}N{\cdot}OH\\ Cl\end{smallmatrix} + 2H_2O = HCO_2H + NH_2OH{\cdot}HCl.$$

Polymerization of Fulminic Acid.—Free fulminic acid is unstable and even in ether or water solution undergoes polymerization with liberation of energy. The principal product is the trimeric metafulminuric acid, first prepared by Scholvien and later shown to have the constitution I (*diisonitrosoisoxazolone*) by Wieland (Ber. **42**, 1346). In much smaller quantity the tetrameride *iso*cyanilic acid is formed, for which Wieland has established the constitution II (*dioxime* of *furoxandialdehyde*) (*Wieland*, Ann. **444**, 7: *Scholvien*, J. pr. Chem. **32**, 477):



(I)
Metafulminuric acid.



(II)
*iso*Cyanilic acid.

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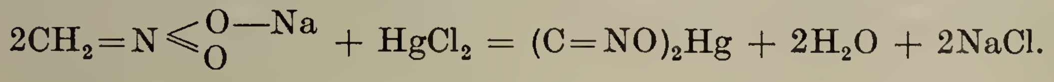
* *H Wieland*, Die Knallsäure, Enke, Stuttgart, 1909.

The fulminuric acid $(C:NOH)_3$ of Liebig (see p. 296) and the so-called *iso*-fulminuric acid of Ehrenberg (J. pr. Chem. **30**, 98), later identified as oxyfurazancarbonamide (Ann. **392**, 196), are secondary products from metafulminuric acid.

The most important of the salts is mercury fulminate, which is employed, technically, as a detonating agent.

Historical.—Mercury fulminate was first obtained by *Howard*, in 1800, by the interaction of a solution of mercuric nitrate and alcohol. In 1824, *Liebig* and *Gay-Lussac* showed that silver fulminate possesses the same percentage composition as silver cyanate, discovered by *Wöhler* in 1822—an observation which paved the way for the recognition of the phenomenon of isomerism (p. 34). *Kekulé* (1856) considered fulminic acid to be nitro-acetonitrile, NO_2CH_2CN, an assumption which could not be sustained, since in 1883 *Ehrenberg* and *Carstanjer*, and also *Steiner*, found that all the nitrogen in fulminic acid appears as hydroxylamine when the acid is treated with hydrochloric acid. *Steiner* ascribed to fulminic acid the formula $C(NOH):C(NOH)$. In 1890, however, *R. Scholl* put forward the formula $C{=}NOH$, indicating that fulminic acid is the oxime of carbon monoxide; this *Nef* completely substantiated in 1894 by thorough experimental investigation (Ber. **33**, 51).

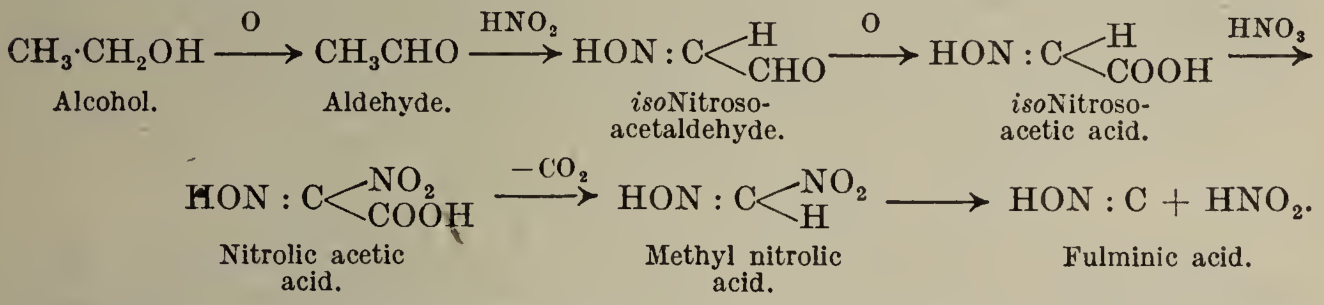
Mercury fulminate, $(C{=}N{\cdot}O)_2Hg + \frac{1}{2}H_2O$ (Ber. **18**, R. 148), is formed (1) by the action of alcohol (Ber. **9**, 787 : **19**, 993, 1370), acetaldehyde, dimethyl acetal or malonic acid (C. 1901, II. 404) on a solution of mercury in excess of nitric acid which contains oxides of nitrogen (Ber. **38**, 1345) ; (2) by the addition of a solution of sodium nitromethane to a mercuric chloride solution :



$$2CH_2{=}N\lessdot\begin{smallmatrix}O{-}Na\\O\end{smallmatrix} + HgCl_2 = (C{=}NO)_2Hg + 2H_2O + 2NaCl.$$

There is always produced at the same time a yellow basic salt, $(Hg\!<\!\begin{smallmatrix}O\\O\end{smallmatrix}\!>\!C{=}NO)_2Hg$, which is the sole product obtained on pouring a solution of mercuric chloride into a solution of sodium nitromethane. This yellow salt is also very explosive.

(3) By boiling methyl nitrolic acid (p. 289) with dilute nitric acid in presence of mercury salts. This reaction indicates the course of the formation of fulminic acid from alcohol (Ber. **40**, 421) :



$$\underset{\text{Alcohol.}}{CH_3{\cdot}CH_2OH} \xrightarrow{O} \underset{\text{Aldehyde.}}{CH_3CHO} \xrightarrow{HNO_2} \underset{\substack{\textit{iso}\text{Nitroso-}\\ \text{acetaldehyde.}}}{HON:C\!<\!\begin{smallmatrix}H\\CHO\end{smallmatrix}} \xrightarrow{O} \underset{\substack{\textit{iso}\text{Nitroso-}\\ \text{acetic acid.}}}{HON:C\!<\!\begin{smallmatrix}H\\COOH\end{smallmatrix}} \xrightarrow{HNO_3}$$

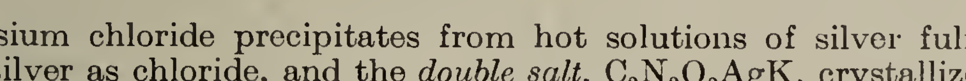
$$\underset{\substack{\text{Nitrolic acetic}\\ \text{acid.}}}{HON:C\!<\!\begin{smallmatrix}NO_2\\COOH\end{smallmatrix}} \xrightarrow{-CO_2} \underset{\substack{\text{Methyl nitrolic}\\ \text{acid.}}}{HON:C\!<\!\begin{smallmatrix}NO_2\\H\end{smallmatrix}} \longrightarrow \underset{\text{Fulminic acid.}}{HON:C} + HNO_2.$$

The formation of fulminic acid from malonic acid (p. 542) proceeds similarly to the above.

Fulminating mercury crystallizes in shining, white needles, which are fairly soluble in hot water. It explodes violently on percussion, and also when acted on by concentrated sulphuric acid. Concentrated hydrochloric acid evolves CO_2, and yields hydroxylamine hydrochloride and formic acid, a reaction well adapted for the preparation of hydroxylamine (Ber. **19**, 993).

Chlorine gas decomposes mercury fulminate into mercuric chloride, cyanogen chloride and CCl_3NO_2. Aqueous ammonia converts it into urea and guanidine (see acetyl *iso*cyanate). Silver fulminate in benzene solution is converted by aluminium chloride into β-benzaldoxime (Ber. **32**, 3492).

Silver fulminate, $C:NOAg$, white needles, is prepared after the manner of the mercury salt, and is even more explosive than the latter. It is also prepared from acetoformyl chloridoxime (p. 289) and $AgNO_3$:

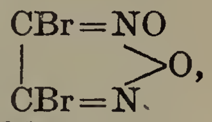


$$\begin{smallmatrix}H\\Cl\end{smallmatrix}\!>\!C{=}NOCOCH_3 \xrightarrow{2AgNO_3} AgCl + CNOAg + HOCOCH_3.$$

Potassium chloride precipitates from hot solutions of silver fulminate one atom of silver as chloride, and the *double salt*, $C_2N_2O_2AgK$, crystallizes from the solution. Nitric acid precipitates from this salt *acid silver fulminate*, $C_2N_2O_2AgH$, a white, insoluble precipitate. On boiling mercury fulminate with water and copper or zinc, metallic mercury is precipitated and copper and zinc fulminates ($C_2N_2O_2Cu$ and $C_2N_2O_2Zn$) are produced.

Sodium fulminate, C : NONa, is obtained when mercury fulminate is digested with sodium amalgam in alcohol. It crystallizes in fine needles, is explosive and poisonous. Examined by the freezing-point method, its molecule is found to be a simple one (Ber. **38**, 1355 : Ann. **298**, 345). A solution acidified with sulphuric acid yields to ether a crystalline explosive acid $(CNOH)_3$. Sodium fulminate is converted to an *ester* $(CNOCH_3)_3$, m.p. 149°, by means of dimethyl sulphate (C. 1907, I. 27).

In the formation of salts and double salts fulminic acid behaves much like hydrocyanic acid. This is readily understood if hydrocyanic acid be regarded as hydrogen *iso*cyanide, C=NH. Sodium ferrocyanide corresponds with *sodium ferrofulminate*, $(C{=}NO)_6FeNa_4 + 18H_2O$, which is produced by bringing together a solution of sodium fulminate and ferrous sulphate (Ann. **280**, 335). It consists of yellow needles.

The compound *dibromofuroxan* (dibromoglyoxime peroxide)  m.p. 50°, regarded by its discoverer Kekulé (Ann. **105**, 291) as *dibromonitroacetonitrile*, is formed by the action of bromine on mercury fulminate. It has later been shown by Wieland to be a furoxan derivative (Ann. **358**, 56 : Ber. **42**, 4192). This body, when heated with hydrochloric acid, passes into HBr, NH_3, NH_2OH and oxalic acid. Aniline probably converts the dibromide into the dioxime of oxanilide $(C_6H_5NHC{=}NOH)_2$.

Fulminuric acid, *Nitrocyanacetamide*, $C_3N_3O_3H_3 = CN{\cdot}CH(NO_2)CONH_2$, is a derivative of tartronic acid. Its alkali salts are obtained by boiling mercuric fulminate with potassium chloride or ammonium chloride and water. The sodium salt is converted, by a mixture of sulphuric and nitric acids, into trinitroacetonitrile. The free acid is obtained by decomposing the lead salt with hydrogen sulphide. It deflagrates at 145°. Especially characteristic is the *cuprammonium salt*, $C_3N_3O_3H_3(CuNH_3)$, which consists of glistening purple-coloured prisms. (Comp. Cyanuric acid.)

Ethyl iodide converts the silver salt at 80–90° into the *ethyl ester*, $C_3H_2N_3O_2(OC_2H_5)$, m.p. 133°, which is changed into **desoxyfulminuric acid**, *cyano*iso*nitroso-acetamide*, $C_3N_3H_3O_2 = CN{\cdot}C(:NOH)CONH_2$, m.p. 184° (Ann. **280**, 331), a mesoxalic acid derivative, when boiled with water and alcohol.

THE FATTY ACIDS, $C_nH_{2n+1}{\cdot}COOH$

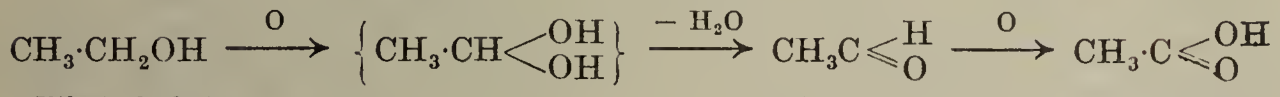
The acids of this series are known as *fatty acids*, because their higher members occur in the natural fats. The latter are esters of the fatty acids, with glycerol, a trihydric alcohol. On boiling them with potassium or sodium hydroxide, alkali salts (soaps) of the fatty acids are formed, and from these the mineral acids liberate the fatty acids. Hence, the process of converting an ester into an acid and an alcohol has been termed saponification. This term, or more usually, and preferably, the term *hydrolysis*, is applied to the conversion of other derivatives of the acids into the acids themselves—*e.g.* the conversion of nitriles into the corresponding acids.

The lower acids (with exception of the first members) are oils ; the higher, commencing with capric acid, are solids at ordinary temperatures. The first can be distilled without decomposition ; the latter are partially decomposed, and can only be distilled without alteration under reduced pressure. Only the first members are volatile in steam. Acids of similar structure show an increase in their boiling points of about 19° for each increase in CH_2. The melting points are higher in acids with an unbranched carbon chain, containing an even number of carbon atoms, than in the case of those having an odd number of carbon atoms. The dibasic acids exhibit the same characteristic. With increase in the length of the carbon chain, the specific gravities of the acids grow successively less, and the acids themselves at the same time approach the hydrocarbons in character. The lower members are readily soluble in water, but the solubility regularly diminishes with increasing molecular weight. All dissolve readily in alcohol, and very easily in ether. Their solutions redden blue litmus. The acidity diminishes with increasing molecular weight; this is very clearly evidenced by the diminution of the heat of neutralization and the initial velocity in the etherification of the acids.

Nomenclature.—The fatty acids can be regarded as substitution products of acetic acid and named accordingly, *e.g.* $CH_3{\cdot}CH_2{\cdot}COOH$ (propionic acid), *methylacetic acid,* $(CH_3)_2CH{\cdot}COOH$ (*iso*butyric acid), *dimethylacetic acid,* etc., similarly to the "carbinol" nomenclature for the alcohols. The higher members of the series with an unbranched carbon chain are described as "normal," *e.g.* $CH_3{\cdot}(CH_2)_4COOH$ as normal or *n*-hexoic acid, and those with a branched chain are preferably named as substitution products of the longest normal chain they contain. Thus, $CH_3(CH_2)_3CH(CH_3){\cdot}COOH$ is conveniently described as α-methylhexoic acid.

The most important general methods of preparation of the monobasic acids are:

(1) Oxidation of the primary alcohols and aldehydes:



$$CH_3{\cdot}CH_2OH \xrightarrow{O} \left\{CH_3{\cdot}CH{<}\begin{matrix}OH\\OH\end{matrix}\right\} \xrightarrow{-H_2O} CH_3C{<}\begin{matrix}H\\O\end{matrix} \xrightarrow{O} CH_3{\cdot}C{<}\begin{matrix}OH\\O\end{matrix}$$

Ethyl alcohol. Aldehyde. Acetic acid.

The oxidizing agents most usually employed are chromic acid and permanganate (C. 1907, I. 1179).

In the presence of a suitable catalyst, such as manganese butyrate, the oxidation of aldehydes to the corresponding acid can be effected by air or oxygen (*e.g.* Butyric acid from butaldehyde, Brit. Pat. 173004, J.C.S. Abstr. 1922, i, 222).

In the case of normal primary alcohols with high molecular weight the conversion into the corresponding acids is effected by heating with soda-lime:

$$\underset{\text{Cetyl alcohol.}}{C_{15}H_{31}CH_2OH} + NaOH = \underset{\text{Sodium palmitate.}}{C_{15}H_{31}{\cdot}CO_2Na} + 2H_2.$$

(2) By the addition of hydrogen to the unsaturated monocarboxylic acids:

$$\underset{\text{Acrylic acid.}}{CH_2{=}CH{\cdot}CO_2H} + 2H = \underset{\text{Propionic acid.}}{CH_3{\cdot}CH_2{\cdot}CO_2H}.$$

(3) By the reduction of hydroxy-acids at raised temperatures by means of hydriodic acid:

$$CH_3{\cdot}CH(OH)CO_2H + 2HI = CH_3{\cdot}CH_2{\cdot}CO_2H + H_2O + I_2.$$

Halogen substituted acids may be reduced by means of sodium amalgam.

Many nucleus-synthetic methods are known for the formation of derivatives of the acids, which can easily be changed to the latter. These methods are important in the building-up of the acids.

(4) *Synthesis of the Acid Nitriles.*—The alkyl cyanides, called also the fatty acid nitriles, are produced by the interaction of potassium cyanide and alkyl halides or the alkali salts of the alkyl sulphuric acids. When the nitriles are heated with alkalis or dilute mineral acids the cyanogen group is transformed into the carboxyl group,

whilst the nitrogen is changed to ammonia. In this manner formic acid is produced from hydrocyanic acid (p. 285) :

$$CH_3\cdot CN + 2H_2O + HCl = CH_3\cdot CO_2H + NH_4Cl$$
$$CH_3\cdot CN + H_2O + KOH = CH_3\cdot CO_2K + NH_3.$$

This method makes the synthesis of acids from alcohols possible.

The normal fatty acids from stearic acid to $C_{26}H_{52}O_2$ have been synthesized by the following series of reactions (J. Biol. Chem. **59**, 905).

$$R\cdot COOR \longrightarrow R\cdot CH_2OH \longrightarrow R\cdot CH_2I \longrightarrow R\cdot CH_2CN \longrightarrow R\cdot CH_2COOH$$

The conversion of the nitriles directly into esters of the acids may be effected by dissolving them in alcohol and passing hydrochloric acid gas into the solution, or by warming it with sulphuric acid (Ber. **9**, 1590).

(5) The action of carbon monoxide on the sodium alcoholates heated to 160–200° only proceeds smoothly and easily in the case of sodium methoxide and ethoxide (Ann. **202**, 294 : C. 1903, II. 933) :

$$\underset{\text{Sodium ethoxide.}}{C_2H_5\cdot ONa} + CO = \underset{\text{Sodium propionate.}}{C_2H_5\cdot CO_2\cdot Na.}$$

Similarly, carbon monoxide and sodium hydroxide yield sodium formate (p. 282).

(6) The action of carbon dioxide on sodium alkyls (Ann. **111**, 234) is only applicable with sodium methyl and sodium ethyl (p. 223).

$$C_2H_5\cdot Na + CO_2 = C_2H_5\cdot CO_2Na.$$

By the action of carbon dioxide on an ethereal solution of an alkyl magnesium halide, and the decomposition of the resulting magnesium compound by ice and sulphuric acid (C. 1901, II. 622 : Ber. **35**, 2519) :

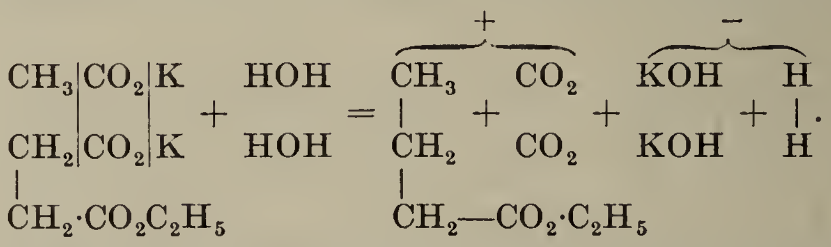
$$CH_3MgBr \xrightarrow{CO_2} CH_3CO_2MgBr \xrightarrow{H_2O} CH_3COOH.$$

(7) By the action of phosgene gas, $COCl_2$, on the zinc alkyls. Acid chlorides are first formed, and subsequently yield acids when treated with water :

$$Zn(CH_3)_2 + 2COCl_2 = \underset{\text{Acetyl chloride.}}{2CH_3\cdot COCl} + ZnCl_2.$$

$$CH_3\cdot COCl + H_2O = \underset{\text{Acetic acid.}}{CH_3\cdot CO\cdot OH} + HCl.$$

(8) Electro-syntheses of the esters of monocarboxylic acids occur upon electrolysing mixtures of the salts of fatty acids and the mono-esters of dicarboxylic acids. Butyric ester, for example, is obtained from potassium acetate and potassium ethyl succinate (Ber. **28**, 2427) :



$$\begin{array}{lcccccc} CH_3|CO_2|K & & HOH & & \overbrace{CH_3 \qquad CO_2}^{+} & & \overbrace{KOH \qquad H}^{-} \\ || & + & & = & | \qquad + & + & \qquad + \; | \, . \\ CH_2|CO_2|K & & HOH & & CH_2 \qquad CO_2 & & KOH \qquad H \\ | & & & & | & & \\ CH_2\cdot CO_2C_2H_5 & & & & CH_2{-}CO_2\cdot C_2H_5 & & \end{array}$$

The following methods of formation are based upon the breaking-down of long carbon chains :

(9) The decomposition of ketones by oxidation with potassium dichromate and sulphuric acid :

$$\underset{\text{Pentadecyl methyl ketone (from palmitic acid.)}}{CH_3[CH_2]_{14}\cdot CO\cdot CH_3} \xrightarrow{O} \underset{\text{Pentadecylic acid.}}{CH_3[CH_2]_{13}CO_2H} + \underset{\text{Acetic acid.}}{CH_3\cdot CO_2H}$$

By the action, also, of alkali hypochlorites and hypobromites, the alkyl methyl ketones can be made to yield chiefly carboxylic acids, the methyl group being split off as chloroform or bromoform.

(10) The trialkylacetophenones (Vol. II) are broken down in benzene solution by the action of sodamide into benzene and the amides of trialkylacetic acids (C. 1909, I. 912: II. 600):

$$C_6H_5{\cdot}CO{\cdot}CR_3 \xrightarrow{NaNH_2} C_6H_6 + R_3C{\cdot}CO{\cdot}NH_2.$$

The hexaalkylacetones are broken down similarly (C. 1910, I. 1698: Ann. Chim. Phys. [9] **1**, 5).

(11) Decomposition of unsaturated acids by fusion with potassium hydroxide:

$$\underset{\text{Potassium angelicate.}}{CH_3CH : C(CH_3)CO_2K} \xrightarrow{KOH} \underset{\text{Potassium acetate.}}{CH_3CO_2K} \text{ and } \underset{\text{Potassium propionate.}}{CH_3CH_2{\cdot}CO_2K.}$$

It is important to note that a shift of the position of the double bond may occur during this alkali fusion, and the breakdown products are not necessarily those which would be obtained if the unsaturated acid had been broken down at the original double linkage.

(12) By cautious oxidation of the higher paraffins by air (Ber. **53**, 66, 987).

(13) Decomposition of acetoacetic ester, as well as mono- and dialkyl acetoacetic esters, by concentrated alcoholic potassium hydroxide:

$$\underset{\text{Acetoacetic ester.}}{CH_3CO{\cdot}CH_2CO_2C_2H_5} + 2KOH = CH_3CO_2K + CH_3CO_2K + C_2H_5OH$$

$$CH_3CO{\cdot}CH(R)CO_2C_2H_5 + 2KOH = CH_3CO_2K + CH_2(R)CO_2K + C_2H_5{\cdot}OH$$
$$CH_3CO{\cdot}C(R)_2CO_2C_2H_5 + 2KOH = CH_3CO_2K + CH(R)_2CO_2K + C_2H_5{\cdot}OH.$$

On account of the readiness with which the mono- and dialkyl acetoacetic esters are prepared, this forms a valuable method for obtaining mono- and dialkylacetic acids (see Acetoacetic ester).

(14) Substituted acid amides, from which the acid may be obtained by hydrolysis, are formed by the Beckmann transformation of ketoximes and oximino-acids, the latter being obtained from the unsaturated acids by converting them into the keto-derivatives of the saturated acids (see Beckmann transformation, p. 268, and oleic acid, p. 349).

(15) By the decomposition of malonic acid and the alkyl derivatives of malonic acid by heat, with loss of CO_2. These acids are dicarboxylic acids, in which both carboxyl groups are attached to the same carbon atom.

$$\underset{\text{Malonic acid.}}{CH_2(COOH)_2} \longrightarrow \underset{\text{Acetic acid.}}{CH_3{\cdot}COOH} + CO_2$$

$$CRR'(COOH)_2 \longrightarrow CHRR'{\cdot}COOH + CO_2.$$

These substituted malonic acids are also readily available, and this method is a valuable one for the preparation of many fatty acids (see Malonic ester).

Isomerism.—Every monocarboxylic acid corresponds with a primary alcohol. Hence the number of isomeric monocarboxylic acids of definite carbon content is, as in the instance of the aldehydes, equal to that of the possible primary alcohols (p. 128), possessing the same number of carbon atoms. The isomerism is dependent upon the isomerism of the hydrocarbon radical in union with the carboxyl group.

There are no possible isomers of the first three members of the series $C_nH_{2n}O_2$:

$H\cdot CO_2H$	$CH_3\cdot CO_2H$	$C_2H_5\cdot CO_2H$
Formic acid.	Acetic acid.	Propionic acid.

Two structural isomers are possible for the fourth member, $C_4H_8O_2$:

$CH_3\cdot CH_2\cdot CH_2\cdot CO_2H$ and	$(CH_3)_2\cdot CH\cdot CO_2H$.
Butyric acid.	*iso*Butyric acid.

Four isomers are possible with the fifth member, $C_5H_{10}O_2 = C_4H_9\cdot CO_2H$, inasmuch as there are four butyl, C_4H_9, groups.

Reactions.—The principal reactions of the fatty acids are the following:

(1) Acids and alcohols yield *esters* in the presence of hydrochloric or sulphuric acid (p. 310).

(2) Salts of fatty acids and alkyl halides, or alkyl sulphates, yield *esters*.

(3) Acids or salts, when acted on by the chlorides of phosphorus, yield *acid chlorides* (p. 314) and *acid anhydrides* (p. 317).

(4) The ammonium salts of the acids lose water when heated or treated with dehydrating agents and yield *acid amides* (p. 321) and *acid nitriles* (p. 324).

(5) The halogens produce substitution products.

(6) The fatty acids are only attacked very slowly by oxidizing agents. Acids containing a tertiary group yield nitro-derivatives when acted on by nitric acid (Ber. **15**, 2318: **32**, 3661).

(7) *Paraffins* result from the reduction of higher fatty acids by hydriodic acid.

(8) *Paraffins* are produced when the calcium salts of the fatty acids are distilled with soda-lime.

(9) *Paraffins*, together with CO_2, alcohols, and other products, result from the electrolysis of concentrated solutions of the potassium salts of the fatty acids.

(10) Acid chlorides and anhydrides, when reduced, yield *aldehydes* and *primary alcohols*.

(11) Acid chlorides, esters, amides, and nitriles reacting with zinc alkyls or magnesium alkyl halides yield *ketones* and *tertiary alcohols*.

(12) By the interaction of iodine and the silver salts of fatty acids, esters of the next lower alcohol are formed.

(13) When the calcium salts are distilled with calcium formate, *aldehydes* are produced.

(14) Simple and mixed *ketones* are formed when a single calcium salt or an equimolecular mixture of two different calcium salts are distilled respectively.

(15) The reduction of acid nitriles yields *primary amines*; these are converted into the corresponding alcohols by nitrous acid.

(16) Acid amides, when acted on by bromine and sodium hydroxide, yield the next lower *primary amine*. This reaction can therefore be employed for proceeding step by step down the series of fatty acids (p. 308). The azides of the acids behave similarly when acted on by water or alcohol.

Acetic acid, $CH_3\cdot COOH$ (*Acidum aceticum*), formed by the spontaneous souring of alcoholic liquids, is the acid which has been longest known. Vinegar and the term "acid" were designated, for example, by the Romans by closely related words. Wood vinegar first became known in the Middle Ages.

Historical.—At the close of the eighteenth century *Lavoisier* recognized the fact that air was necessary for the conversion of alcohol into acetic acid, and that its volume was correspondingly diminished during the process. In 1830 *Dumas* converted the acid, by means of chlorine, into trichloroacetic acid; whilst the reconversion of the latter into the parent acid, by potassium amalgam and water, was demonstrated by *Melsens* in 1842. When, in 1843, *Kolbe* succeeded in producing trichloroacetic acid (p. 334) from its elements, the first synthesis of acetic acid was accomplished.

Acetic acid is found in the vegetable kingdom both free and in the form of salts and esters, Thus, it was mentioned under *n*-hexyl and *n*-octyl alcohols that they occurred in the form of their acetic esters in the ethereal oil of the seed of *Heracleum giganteum* and in the fruit of *Heracleum sphondylium*. The officinal, concentrated acid, as well as the 30% aqueous solution of the acid, are applied medicinally.

Acetic acid is produced in the decay of many organic substances and in the dry distillation of wood, sugar, tartaric acid, and other compounds; also in the oxidation of numerous carbon derivatives, as it is very stable towards oxidants.

The methods of forming acetic acid, which have any theoretical interest, have already been discussed under the general methods for the production of fatty acids; therefore they will be but briefly noticed here:

(1) The oxidation of ethyl alcohol and acetaldehyde.

(2) The reduction of hydroxyacetic acid or glycollic acid, $CH_2(OH)\cdot CO_2H$, and the reduction of chlorinated acetic acids—*e.g.* trichloroacetic acid, $CCl_3\cdot CO_2H$.

Synthetically: (3) From methyl cyanide or acetonitrile.

(4) From sodium methoxide and carbon monoxide.

(5) From sodium methyl or magnesium methyl iodide and carbon dioxide.

(6) From phosgene and zinc methyl.

By degradation: (7) By the oxidation of acetone and many mixed methyl ketones.

(8) By the decomposition of many unsaturated acids of the oleic series when fused with potassium hydroxide.

(9) From acetoacetic ester by means of alcoholic potassium hydroxide.

(10) By heating malonic acid.

(11) A rather remarkable synthesis consists in allowing air and potassium hydroxide to act on acetylene in diffused daylight (*Berthelot*, 1870):

$$CH \equiv CH + H_2O + O = CH_3\cdot COOH.$$

Preparation.—(1) Acetic acid is produced by the oxidation of ethyl alcohol and liquids containing this alcohol. It is customary, depending upon their origin, to distinguish *wine vinegar*, *fruit vinegar*, and *malt vinegar*.

Quick-vinegar process. (*Schutzenbach*, 1823.)—According to Wieland's views (p. 224), the acetic fermentation of alcoholic liquids consists in a dehydrogenation of the alcohol by the "mother of vinegar" (*Mycoderma aceti*, *Micrococcus aceti* or *Bacterium aceti*), the activated alcohol being then oxidized to water by atmospheric oxygen. The organisms responsible for this action are always present in the air. In this process, by an enlargement of the contact surface of the alcoholic liquid with the air, there ensues an accelerated oxidation. Large wooden tubs are filled with shavings previously moistened with vinegar, upon which diluted (10%) alcoholic solutions are poured. The lower part of the tub, exposed in a warm room (25–30°), is provided with a sieve-like bottom, and all about it are holes permitting the entrance of air to the interior. The liquid collecting on the bottom is run through the same process two or three times, to ensure the conversion of all the alcohol into acetic acid.

(2) *Wood-vinegar process.*—Considerable quantities of acetic acid are also obtained by the dry distillation of wood in cast-iron retorts, a process already referred to when discussing methyl alcohol (p. 136). The aqueous distillate, consisting of acetic acid, wood spirit, acetone, and empyreumatic oils, is neutralized with lime, evaporated to dryness, and the residual calcium salt heated to 230–250°. In this manner, the greater portion of the various organic admixture is destroyed, calcium acetate remaining unaltered. The salt purified in this way is distilled with sulphuric acid, when acetic acid is set free and purified by further distillation over potassium chromate.

(3) At the present day, pure acetic acid is manufactured by the catalytic oxidation of acetaldehyde, obtained from acetylene (see p. 113), vanadium pentoxide being employed as catalyst.

Properties.—Anhydrous acetic acid at low temperatures consists of a leafy, crystalline mass—*glacial acetic acid*—which, on melting at 16·7°, forms a liquid of sharp and penetrating odour. It boils at 118° and has $D_{20} = 1{\cdot}0497$ (see J.C.S. **99**, 1432). It mixes with water in all proportions; at first a contraction ensues, consequently the specific gravity increases until the composition of the solution corresponds with the *hydrate*, $C_2H_4O_2 + H_2O$ $(=CH_3{\cdot}C(OH)_3)$, $D_{15} = 1{\cdot}0748$ (77–80%). On further dilution, the specific gravity becomes less, until a 43% solution possesses about the same specific gravity as anhydrous acetic acid. Ordinary vinegar contains about 5% of acetic acid. Acetic acid is an excellent solvent for many carbon compounds. The halogen acids also dissolve readily in glacial acetic acid (Ber. **11**, 1221). Pure acetic acid should not decolorize a drop of potassium permanganate solution. It may be detected by conversion into volatile acetic ester when heated with alcohol and sulphuric acid, or by the formation of cacodyl oxide (p. 210) when its potassium salt is distilled with arsenious oxide.

Acetates.—The acid combines with one equivalent of the bases, forming readily soluble, crystalline salts. It also forms basic salts with iron, aluminium, lead and copper; these are sparingly soluble in water. The alkali salts have the additional property of combining with a molecule of acetic acid, yielding *acid salts*, such as $C_2H_3O_2K + C_2H_4O_2$, acid potassium acetate.

Potassium acetate, $C_2H_3O_2K$, deliquesces in the air and dissolves readily in alcohol. The *acid* salt, $C_2H_3KO_2{\cdot}C_2H_4O_2$, m.p. 148°, crystallizes out in pearly leaflets. The *salt*, $C_2H_3O_2K + 2C_2H_4O_2$, m.p. 112°, is decomposed at 170° into acetic acid and the neutral salt.

Sodium acetate, $C_2H_3O_2Na + 3H_2O$, crystallizes in large, rhombic prisms, which effloresce on exposure. The *anhydrous salt* is dimorphic (Ber. **46**, 3199). It melts without decomposition at about 320°.

Ammonium acetate, $C_2H_3O_2NH_4$, is a crystalline mass. Heat applied to the dry salt converts it into water and acetamide.

Calcium acetate, $(C_2H_3O_2)_2Ca + H_2O$, and *barium acetate*, $(C_2H_3O_2)_2Ba + H_2O$, dissolve readily in water.

Ferrous acetate, $(C_2H_3O_2)_2Fe$, readily oxidizes in aqueous solution to insoluble basic ferric acetate. *Ferric acetate*, $(C_2H_3O_2)_6Fe_2$, is not crystallizable. The deep-red solutions obtained by mixing a solution of a ferric salt with an acetate contain the mono- and di- acetates of the hexaacetatotriferric base $[Fe_3{}^{(OAc)_6}_{(OH)_2}]OAc$ and $[Fe_3{}^{(OAc)_6}_{(OH)}](OAc)_2$ $(Ac{=}CH_3{\cdot}CO{\cdot})$ (Z. anorg. Chem. **66**, 157). On boiling these solutions, sufficiently dilute, all the iron is precipitated in the form of basic salts. *Aluminium acetate* behaves similarly. Both salts are employed as mordants in dyeing, as they are capable of uniting with the cotton fibre. The basic salts produced on the application of heat are capable of retaining dyes.

Lead acetate, $(C_2H_3O_2)_2Pb + 3H_2O$, is obtained by dissolving litharge in acetic acid. The salt forms brilliant four-sided prisms, which effloresce on exposure. It possesses a sweet taste (hence called *sugar of lead*), and is poisonous. If an aqueous solution of lead acetate be boiled with litharge, *basic lead acetates*, of varying lead content, *e.g.* $C_2H_3O_2PbOH$ and $C_2H_3O_2Pb{\cdot}O{\cdot}Pb{\cdot}O{\cdot}Pb{\cdot}C_2H_3O_2$, are produced. These solutions react alkaline, and absorb carbon dioxide from the air, depositing basic carbonates of lead—white lead.

Lead tetraacetate, $(C_2H_3O_2)_4Pb$, is obtained when minium is dissolved in hot glacial acetic acid. From the filtrate colourless monoclinic crystals, m.p. 175°, separate (Ber. **53**, 485). It is used as an oxidizing agent for organic substances (see Ber. **56**, 1375).

Copper acetate, $(C_2H_3O_2)_2Cu + H_2O$, is easily soluble in water. *Basic copper salts* occur in commerce under the name of *verdigris*. They are obtained by dissolving copper strips in acetic acid in presence of air. The double salt of acetate and arsenite of copper is the so-called *Schweinfurt Green*.

Silver acetate, $C_2H_3O_2Ag$, separates in brilliant needles or leaflets. The salt is soluble in 98 parts water at 14° C.

The decompositions of the acetates have already been considered; summarized they are:

(1) Potassium acetate, when electrolysed, yields *ethane*.

(2) Sodium acetate, heated with soda-lime, yields *methane*.

(3) Potassium acetate and arsenious oxide, on heating, yield *cacodyl oxide*.

(4) Ammonium acetate loses water, when heated, with the formation of *acetamide*.

(5) Calcium acetate is decomposed by heat into *acetone*.

(6) Calcium acetate and calcium formate, heated together, yield *aldehyde*.

(7) Calcium acetate and the calcium salts of higher fatty acids, when heated, yield mixed *methyl alkyl ketones*.

PROPIONIC ACID. BUTYRIC ACIDS. VALERIC ACIDS

The following table contains the melting points (Ber. **29**, R. 344), the boiling points, and the specific gravities of the normal acids and their isomers:

Name.	Formula.	M.P.	B.P.	Specific Gravity.
Propionic acid	$CH_3CH_2—CO_2H$	– 36·5°	140°	0·9920 (18°)
n-Butyric acid	$CH_3(CH_2)_2CO_2H$	—	163°	0·9587 (20°)
*iso*Butyric acid. . . .	$(CH_3)_2CH—CO_2H$	– 79°	155°	0·9490 (20°)
n-Valeric acid	$CH_3(CH_2)_3CO_2H$	– 59°	186°	0·9568 (0°)
*iso*Valeric acid	$(CH_3)_2{\cdot}CH{\cdot}CH{\cdot}CO_2H$	– 51°	174°	0·9470 (0°)
Methylethylacetic acid .	$C_2H_5{\cdot}CH(CH_3){\cdot}CO_2H$	—	175°	0·9410 (21°)
Trimethylacetic acid (Pivalic acid)	$(CH_3)_3C{\cdot}CO_2H$	+ 35°	163°	—

Propionic acid, *Methylacetic acid* [Propane acid], $CH_3{\cdot}CH_2{\cdot}CO_2H$, may be prepared by the methods in general use in making fatty acids; (1) by the oxidation of *n*-propyl alcohol and propionaldehyde with chromic acid; (2) by reduction of acrylic acid (p. 342) and propargylic acid (p. 351); (3) by reduction of lactic acid, $CH_3{\cdot}CH(OH){\cdot}CO_2H$, and glyceric acid, $CH_2OH{\cdot}CHOH{\cdot}CO_2H$; (4) from ethyl alcohol by its conversion, through ethyl iodide, into ethyl cyanide or propionitrile; (5) from sodium ethoxide and carbon monoxide; (6) from sodium ethyl or magnesium ethyl bromide and carbon dioxide; (7) in the oxidation of methyl ethyl, methyl propyl and diethyl ketones: (8) by the action of alcoholic potassium hydroxide on methylacetoacetic ester with the simultaneous production of methyl ethyl ketone; (9) from methylmalonic acid by the application of heat.

Its formation from calcium malate and lactate by fermentation is worthy of note (Ber. **12**, 479 : **17**, 1190). It is also formed by the fermentation of certain hexoses (*q.v.*) by special micro-organisms. *Gottlieb* first discovered propionic acid in 1847, when he fused sucrose with potassium hydroxide. *Dumas* gave the acid its name, derived from πρῶτος, *the first*, πίων, *fat*, because when treated in aqueous solution with calcium chloride it separated as an oil. It is the first acid which in its behaviour approaches the higher fatty acids.

The *barium salt*, $(C_3H_5O_2)_2Ba + H_2O$, crystallizes in rhombic prisms: *silver salt*, $C_3H_5O_2Ag$, dissolves sparingly in water.

Butyric Acids, $C_4H_8O_2$.—(1) **Normal butyric acid**, *Ethylacetic acid* [Butane acid], *butyric acid of fermentation*, occurs free and also as the glycerol ester in the vegetable and animal kingdoms, especially in the butter of cows (to the amount of about 5% together with glycerides of palmitic and oleic acids), in which Chevreul found it, in the course of his classic investigations upon the fats. It exists as hexyl ester in the oil of *Heracleum giganteum*, and as octyl ester in *Pastinaca sativa*. It has been observed free in the perspiration and in the body fluids. It may be obtained by the usual methods employed for the preparation of fatty acids, and is produced in the butyric fermentation of sugar, starch and lactic acid, and in the decay and oxidation of proteins.

Ordinarily the acid is obtained by the fermentation of sugar or starch, induced by the previous addition of decaying substances, *e.g.* cheese, in the presence of calcium or zinc carbonate, which are intended to neutralize the acids as they form. According to Fitz, the butyric fermentation of glycerol or starch is most advantageously evoked by the direct addition of bacteria, especially *Bacillus subtilis* and *Bacillus boocopricus* (Ber. **11**, 49, 53: **29**, 2726).

Pyruvic acid and acetaldehyde are important intermediate products in this butyric fermentation (Ber. **55**, 3635). Under the action of the synthesizing ferment carboligase, two molecules of pyruvic acid undergo an aldol condensation, from which butyric acid is derived by decarboxylation followed by a Cannizzaro reaction. The idealized butyric fermentation takes place according to the equation:

$$C_6H_{12}O_6 \longrightarrow 2CO_2 + 2H_2 + C_4H_8O_2.$$

Butyric acid is a thick, rancid-smelling liquid, which solidifies when cooled. It dissolves readily in water and alcohol, and may be thrown out of solution by salts.

The *calcium salt*, $(C_4H_7O_2)_2Ca + H_2O$ (Ann. **213**, 67), yields brilliant leaflets and is less soluble in hot than in cold water (in 3·5 parts at 15°); therefore the cold saturated solution grows turbid on warming (Ber. **30**, 2956).

(2) *iso***Butyric acid**, *Dimethylacetic acid* [Methylpropane acid], $(CH_3)_2{\cdot}CH{\cdot}CO_2H$, is found free in St. John's Bread, the pod of the carob- or locust-tree, *Ceratonia siliqua*, as octyl ester in the oil of *Pastinaca sativa*, and as ethyl ester in croton oil. It is prepared according to the general methods. Concentrated nitric acid converts it into ββ-dinitropropane (p. 185); potassium permanganate oxidizes it to α-hydroxy*iso*butyric acid.

*iso*Butyric acid bears great similarity to normal butyric acid, but is not miscible with water.

The *calcium salt*, $(C_4H_7O_2)_2Ca + 5H_2O$, dissolves more readily in hot than in cold water.

Valeric Acids, C_4H_9COOH.—See table, p. 303. Valeric acid occurs free, and as esters in the animal and vegetable kingdoms, chiefly in the small valerian root (*Valeriana officinalis*), and in the root of *Angelica Archangelica*, from which it may be isolated by boiling with water or a soda solution. The natural acid is a mixture of *iso*valeric acid with the optically active methylethylacetic acid, and is therefore also active. A similar artificial mixture may be obtained by oxidizing the amyl alcohol of fermentation (p. 147) with chromic acid mixture. Valeric acid combines with water and yields a hydrate, $C_5H_{10}O_2 + H_2O$, soluble in 26·5 parts of water at 15°.

(1) **Normal valeric acid**, $CH_3(CH_2)_3COOH$, is prepared according to the standard methods.

(2) *iso***Valeric acid**, iso*Propylacetic acid* [3-Methyl-butane acid], $(CH_3)_2{\cdot}CH{\cdot}CH_2{\cdot}CO_2H$, may be synthetically obtained by some of the methods described on pp. 297–299. It is an oily liquid with an odour resembling that of valerian.

Potassium permanganate oxidizes *iso*valeric acid to β-hydroxy*iso*valeric acid, $(CH_3)_2{\cdot}C(OH){\cdot}CH_2{\cdot}CO_2H$. Concentrated nitric acid attacks, in addition, the CH-group, forming methylhydroxysuccinic acid, β-nitro*iso*valeric acid, $(CH_3)_2{\cdot}C(NO_2){\cdot}CH_2{\cdot}CO_2H$, and ββ-dinitropropane, $(CH_3)_2C(NO_2)_2$ (Ber. **15**, 2324. (*Cf.* *iso*butyric acid).

The iso*valerates* generally have a greasy feel. When thrown in small pieces upon water they have a rotary motion, dissolving at the same time; *barium salt*,

$(C_5H_9O_2)_2Ba$; *calcium salt*, $(C_5H_9O_2)_2Ca + 3H_2O$, forms stable, readily soluble needles ; *zinc salt*, $(C_5H_9O_2)_2Zn + 2H_2O$, crystallizes in large, brilliant leaflets ; when the solution is boiled a basic salt separates.

(3) **Methylethylacetic acid**, [2-Methyl-butane acid], $C_2H_5\cdot\overset{*}{C}H(CH_3)\cdot CO_2H$, contains an asymmetric carbon atom, and, like its corresponding alcohol (p. 147), may exist in two optically active and one optically inactive modification. The optically inactive form has been synthesized, and has been resolved by means of its brucine salts into its optically active components. The *l*-salt dissolves with difficulty. The specific rotatory power of the optically active methylethylacetic acid is $[\alpha]_D = \pm 17° 85'$ (Ber. **32**, 1089).

Calcium salt, $(C_5H_9O_2)_2Ca + 5H_2O$.

Optically active methylethylacetic acid is present in valerian and angelica roots together with *iso*valeric acid, as already mentioned, and also in the products of oxidation of fermentation amyl alcohol (Ann. **204**, 159). Pure *d*-methylethylacetic acid is prepared by the oxidation of pure *l*-amyl alcohol (p. 147) (Ber. **37**, 1045) ; and has been found in the breakdown products of convolvulin (Vol. II).

(4) **Trimethylacetic acid**, *Pivalic acid*, [Dimethyl-propane acid], $(CH_3)_3$-$C\cdot CO_2H$), is formed from *tert.*-butyl iodide, $(CH_3)_3CI$ (p. 163), by means of the cyanide ; also by the oxidation of pinacolin (p. 265), or by the breakdown of trimethyl acetophenone and hexamethylacetone by sodamide (see p. 299). The acid is soluble in 40 parts H_2O at 20°, and has an odour resembling that of acetic acid.

Barium salt, $(C_5H_9O_2)_2Ba + 5H_2O$; *calcium salt*, $(C_5H_9O_2)_2Ca + 5H_2O$ (C. 1898, I. 202).

HIGHER FATTY ACIDS

The subjoined table contains the melting and boiling points of some of the higher fatty acids, the boiling points in parentheses being determined under 100 mm. pressure.

Name.	Formula.	M.P.	B.P.
n-Hexoic acid (Caproic acid) .	$CH_3(CH_2)_4\cdot COOH$	+ 8°	205°
*iso*Butylacetic acid. . . .	$(CH_3)_2CH(CH_2)_2\cdot COOH$	—	198°
sec.-Butylacetic acid . . .	$C_2H_5\cdot CHMe\cdot CH_2\cdot COOH$	—	174°
Diethylacetic acid	$(C_2H_5)_2CH\cdot COOH$	—	190°
Methylpropylacetic acid . .	$CH_3(CH_2)_2\cdot CHMe\cdot COOH$	—	193°
Methyl*iso*propylacetic acid .	$CHMe_2\cdot CHMe\cdot COOH$	—	191°
Dimethylethylacetic acid . .	$CMe_2Et\cdot COOH$	− 14°	187°
n-Heptoic acid (Œnanthic acid)	$CH_3\cdot(CH_2)_5\cdot COOH$	− 10·5°	223°
Methylbutylacetic acid . .	$CH_3\cdot(CH_2)_3\cdot CHMe\cdot COOH$	—	210°
Ethylpropylacetic acid . .	$CH_3(CH_2)_2\cdot CHEt\cdot COOH$	—	209°
Methyldiethylacetic acid . .	$CMeEt_2\cdot COOH$	—	208°
n-Octoic acid (Caprylic acid) .	$CH_3(CH_2)_6\cdot COOH$	16·5°	237°
n-Nonoic acid (Pelargonic acid)	$CH_3(CH_2)_7\cdot COOH$	12·5°	254°
n-Decoic acid (Capric acid) .	$CH_3(CH_2)_8\cdot COOH$	31·4°	270°
n-Undecoic acid	$CH_3(CH_2)_9\cdot COOH$	28·5°	(212·5°)
n-Dodecoic acid (Lauric acid)	$CH_3(CH_2)_{10}\cdot COOH$	43·5°	(225°)
n-Tridecoic acid	$CH_3(CH_2)_{11}\cdot COOH$	40·5°	(236°)
n-Tetradecoic acid (Myristic acid)	$CH_3(CH_2)_{12}\cdot COOH$	53·8°	(220·5°)
n-Pentadecoic acid . . .	$CH_3(CH_2)_{13}\cdot COOH$	51°	(260°)
n-Hexadecoic acid (Palmitic acid)	$CH_3(CH_2)_{14}\cdot COOH$	62°	(278·5°)
n-Heptadecoic acid . . .	$CH_3(CH_2)_{15}\cdot COOH$	59·9°	(280·5°)
n-Octadecoic acid (Stearic acid)	$CH_3(CH_2)_{16}\cdot COOH$	69·2°	(291°)
Arachidic acid	$CH_3(CH_2)_{18}\cdot COOH$	75°	—
Behenic acid	$C_{22}H_{44}O_2$	83°	—
Cerotic acid	$C_{26}H_{52}O_2$ or $C_{27}H_{54}O_2$	78°	—
Melissic acid	$C_{30}H_{60}O_2$	90°	—

X-ray spectra of the higher fatty acids, see J.C.S. **1926,** 2310.

A number of acids of the type $CH_3\cdot(CH_2)_n\cdot CHMe\cdot COOH$ have been prepared (J. Soc. Chem. Ind. **46,** 152T).

A large number of fatty acids of the general type CHRR′·COOH have been synthesized by Adams and his colleagues (J.A.C.S. **52,** 1289).

For the normal fatty acids from C_{18} to C_{26}, see J. Biol. Chem. **59,** 905.

The fatty acids which occur naturally in oils, fats and waxes are almost entirely those with an unbranched carbon chain containing an even number of carbon atoms.

Caproic acid, n-*Hexoic acid,* $CH_3(CH_2)_4CO_2H$, occurs in the form of its glyceryl ester in cow's butter, goat butter, and in coconut oil. It is produced, together with butyric acid, in the butyric fermentation.

Œnanthylic acid, n-*Heptoic acid,* $CH_3(CH_2)_5CO_2H$, can easily be obtained as an oxidation product of œnanthol (p. 238).

Caprylic acid, n-*Octoic acid,* $CH_3(CH_2)_6CO_2H$, occurs as its glyceryl ester in goat butter and in many fats and oils; also in the fusel-oil of wine.

Pelargonic acid, n-*Nonoic acid,* $CH_3(CH_2)_7CO_2H$, is present in the leaves of *Pelargonium roseum,* and is prepared by the oxidation of oleic acid and oil of rue (methyl *n*-nonyl ketone, p. 265). It may also be obtained by the fusion of undecylenic acid with potassium hydroxide.

n-Decoic acid, *Capric acid,* $CH_3(CH_2)_8COOH$, is the first acid solid at ordinary temperatures. Preparation of pure decoic acid, J.C.S. **1931,** 2046. It is present as glyceride in butter, goat butter, coconut oil and other fats, and as amyl ester in fusel oil.

n-Undecoic acid, $CH_3(CH_2)_9CO_2H$, is obtained by reduction of undecylenic acid from castor oil.

Lauric acid, n-*Dodecoic acid,* $CH_3(CH_2)_{10}CO_2H$, occurs as its glyceryl ester in the fruit of laurels, *Laurus nobilis,* in coconut oil (C. 1904, I. 259), and in pichurim beans. It is found as its *cetyl ester* in spermaceti.

Myristic acid, n-*Tetradecoic acid,* $CH_3\cdot(CH_2)_{12}CO_2H$, occurs in muscat butter (from *Myristica moschata*), in spermaceti and coconut, in *myristin* (Ber. **18,** 2011 : **19,** 1435), in earth-nuts (Ber. **22,** 1743), in ox-bile (Ber. **25,** 1829), and as free acid, as well as its methyl ester, in iris root (Ber. **26,** 2677).

Palmitic acid, n-*Hexadecoic acid,* $CH_3(CH_2)_{14}CO_2H$.—The glyceryl ester of this acid and that of stearic acid and oleic acid are the principal constituents of solid animal fats. Palmitic acid occurs in rather large quantities, partly uncombined, in palm oil. Spermaceti is the *cetyl ester* of the acid, whilst the *myricyl ester* is the chief constituent of beeswax. The acid is most advantageously obtained from olive oil, which consists almost exclusively of the glycerides of palmitic and oleic acids; also, from Japan wax, a glyceride of palmitic acid (Ber. **21,** 2265). The acid is artificially made by heating cetyl alcohol with soda-lime to 270°; also by fusing together oleic acid and potassium hydroxide.

Margaric acid, n-*Heptadecoic acid,* $CH_3(CH_2)_{15}CO_2H$, does not apparently exist naturally in the fats (Ber. **38,** 1247). It is made in the laboratory by boiling cetyl cyanide with potassium hydroxide. Preparation from stearic acid, Ber. **56,** 1736. An artificial fat, "*intarvin,*" containing glycerides of heptadecoic acid has been used in the treatment of diabetes. (See Kahn, Proc. Soc. Exp. Biol. and Med. 1922, **19,** 265.)

Stearic acid, n-*Octodecoic acid,* $CH_3(CH_2)_{16}CO_2H$, is associated with palmitic and oleic acids as a mixed glyceride in solid animal fats—the tallows. Its name is derived from στέαρ = tallow. It can be obtained by the hydrogenation of oleic acid in presence of finely divided platinum, palladium or nickel (see p. 349).

Arachidic acid, *Eicosoic acid,* $CH_3(CH_2)_{18}COOH$, occurs in earth-nut oil (from *Arachis hypogea*). Preparation, see J.C.S. **127**, 70. *Theobromic acid,* m.p. 72°, from cacao butter appears to be identical with arachidic acid.

Behenic acid, $C_{22}H_{44}O_2$, occurs in the oil from *Moringa oleifera* and is prepared by the reduction of erucic acid (Ber. **27**, R. 577 : C. 1897, II. 1101 : Monatsh. **34**, 1113).

Lignoceric acid, $C_{24}H_{47}O_2$, occurs as glyceride in *Arachis* oil and free in the tar from beech wood and brown coal It contains a branched carbon chain (Monatsh. **34**, 1113 : Ber. **59**, 36). It is formed by the oxidation of cerebronic acid with permanganate in acetone (J. Biol. Chem. **26**, 115).

Cerotic acid, $C_{26}H_{52}O_2$ (Ber. **30**, 1418), occurs together with melissic acid, in a free condition in beeswax, and may be extracted from this by means of boiling alcohol. As its ceryl ester, it is the chief constituent of *Chinese wax* (Ber. **30**, 1415). Its name is derived from *cera* = wax. An apparently identical acid has been obtained from *Arachis* oil (Ber. **59**, 36).

An acid, $C_{26}H_{52}O_2$ (**phthioic acid**), has been obtained from tubercle bacilli (*Anderson,* J. Biol. Chem. **85**, 77).

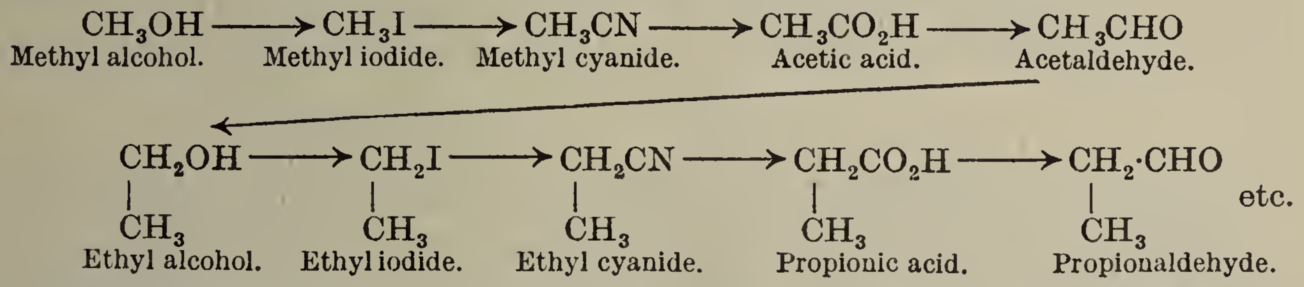
Montanic acid, $C_{28}H_{56}O_2$, occurs partly as ester, partly as free acid in the so-called " *Montan-wax* " from brown coal distillation (Monatsh. **34**, 1143).

Melissic acid, $C_{30}H_{60}O_2$, m.p. 88°, is formed from myricyl alcohol (p. 149) when the latter is heated with soda-lime. It is a waxy substance, and appears to be a mixture of two acids.

The acids mentioned in the table, but not described here, have been prepared by the usual synthetic methods. Some of them will be encountered later in the form of oxidation or reduction products of complicated, complex aliphatic derivatives.

Synthesis and Degradation of the Fatty Acids

Synthesis.—The synthetic methods for the production of the fatty acids are not all equally well adapted for this purpose. Reactions especially fitted for the synthesis of the higher mono- and dialkylacetic acids, are based on the behaviour of acetoacetic ester and malonic ester (methods 13 and 15). Trialkylacetic acids cannot be synthesized in this way. The nitriles of the latter, *e.g.* of trimethylacetic acid, are obtained from the iodides of the corresponding tertiary alcohols. The nitrile synthesis renders the formation of acids from alcohols possible, and inasmuch as acids can be reduced to aldehydes and alcohols by the reduction of the acid chlorides (p. 314), the synthesis of these two classes of bodies is made possible. *Lieben, Rossi,* and *Janecek* (Ann. **187**, 126), beginning with methyl alcohol, systematically prepared the normal acids and corresponding alcohols up to œnanthic acid, according to the following scheme :



$$\underset{\text{Methyl alcohol.}}{CH_3OH} \longrightarrow \underset{\text{Methyl iodide.}}{CH_3I} \longrightarrow \underset{\text{Methyl cyanide.}}{CH_3CN} \longrightarrow \underset{\text{Acetic acid.}}{CH_3CO_2H} \longrightarrow \underset{\text{Acetaldehyde.}}{CH_3CHO}$$

$$\underset{\text{Ethyl alcohol.}}{\begin{array}{l}CH_2OH\\ |\\ CH_3\end{array}} \longrightarrow \underset{\text{Ethyl iodide.}}{\begin{array}{l}CH_2I\\ |\\ CH_3\end{array}} \longrightarrow \underset{\text{Ethyl cyanide.}}{\begin{array}{l}CH_2CN\\ |\\ CH_3\end{array}} \longrightarrow \underset{\text{Propionic acid.}}{\begin{array}{l}CH_2CO_2H\\ |\\ CH_3\end{array}} \longrightarrow \underset{\text{Propionaldehyde.}}{\begin{array}{l}CH_2{\cdot}CHO\\ |\\ CH_3\end{array}} \quad \text{etc.}$$

Degradation.—The following reactions are of importance in the degradation of the normal fatty acids :

(1) The formation (9, p. 298) of carboxylic acids by the oxidation of mixed methyl *n*-alkyl ketones, in which the CO-group remains in combination with the methyl group.

(2) The reaction (15, p. 191) of acid amides with bromine and potassium hydroxide.

(3) The action of alkalis on the α-bromo acid amides.

(4) The oxidation of the ammonium salts with hydrogen peroxide.

(5) The action of iodine on the silver salts.

(6) The oxidation of the olefinecarboxylic acids, produced by bromination and subsequent abstraction of HBr.

(7) The heating of α-hydroxy-fatty acids, obtained from α-bromo-fatty acids, whereby the next lower aldehyde is obtained (*cf.* p. 413).

(8) Oxidation of the tertiary alcohol, or of the olefine formed by loss of water from the alcohol, obtained by the action of magnesium methyl iodide on the esters.

Examples of these Degradation Reactions.—1. The first of these reactions was employed systematically by *F. Krafft* for the breaking-down of stearic acid into normal fatty acids of known constitution, from which it was concluded that stearic acid and the lower homologues derived from it possessed normal constitution. Upon distilling barium stearate, $(C_{17}H_{35}CO_2)_2Ba$, and barium acetate, $(CH_3CO_2)_2Ba$, methyl heptadecyl ketone, $C_{17}H_{35}COCH_3$, results. When this is oxidized it breaks down into margaric acid, $C_{16}H_{33}CO_2H$, and acetic acid. Barium margarate and barium acetate yield methyl hexadecyl ketone, $C_{16}H_{33}{\cdot}CO{\cdot}CH_3$, and this, by oxidation, passes into palmitic acid, $C_{15}H_{31}CO_2H$, and acetic acid, etc.:

$$\begin{tikzcd}
\underset{\text{Barium stearate.}}{(C_{17}H_{35}CO_2)_2Ba} \arrow[r, "(CH_3CO_2)_2Ba", "\text{distil}"'] & C_{17}H_{35}COCH_3 \arrow[r, "CrO_3"] & \underset{\text{Margaric acid.}}{C_{16}H_{33}CO_2H} \arrow[dll] \\
\underset{\text{Barium margarate.}}{(C_{16}H_{33}CO_2)_2Ba} \arrow[r] & C_{16}H_{33}COCH_3 \arrow[r] & \underset{\text{Palmitic acid.}}{C_{15}H_{31}CO_2H}
\end{tikzcd}$$

2. *A. W. Hofmann* (Ber. **19**, 1433) discovered the second method, which will be treated more fully in connection with the acid amides and nitriles (pp. 190, 321); here only the diagrammatic representation of the course of reaction need be given. When the acid amides are treated with bromine and sodium hydroxide they lose the CO-group in the form of CO_2 and pass into the next lower primary amines, which, by further treatment with the same reagents, become converted into the nitrile of a carboxylic acid containing an atom less of carbon, and its amide is still capable of a like transformation. By this method the higher, more easily obtained, normal fatty acids can be changed into lower acids:

$$\underset{\text{Myristamide.}}{C_{13}H_{27}CONH_2} \longrightarrow \underset{\text{Tridecylamine.}}{C_{13}H_{27}NH_2} \longrightarrow \underset{\text{Tridecyl nitrile.}}{C_{12}H_{25}CN} \longrightarrow \underset{\text{Tridecylamide.}}{C_{12}H_{25}CONH}$$

The degradation of the acid hydrazides, via the azides, to urethanes leads to the same result (Curtius, Ber. **27**, 779: **29**, 1166).

(3) The α-bromo-acid amides break down when heated with potassium hydroxide into HCN, HBr and an aldehyde or ketone containing one carbon atom less (Monatsh. **29**, 69):

$$R{\cdot}CHBr{\cdot}CONH_2 \longrightarrow R{\cdot}CHO + HCN + HBr.$$

(4) The ammonium salts of fatty acids, when warmed with dilute hydrogen peroxide, yield a ketone containing one carbon atom less, the chain being oxidized in the β-position (J. Biol. Chem. **49**, 123: *cf.* Am. Chem. J. **44**, 41). This reaction resembles the probable β-oxidation of fatty acids which occurs in the animal body:

$$R{\cdot}CH_2{\cdot}CH_2{\cdot}COONH_4 \longrightarrow R{\cdot}CO{\cdot}CH_3.$$

(See also *Dakin*, Oxidations and Reductions in the Animal Body, London, 1922: Z. physiol. Chem. **67**, 490.)

(5) The silver salts of the fatty acids yield the ester of the next lower alcohol, with loss of CO_2 when warmed with iodine (Monatsh. **13**, 320: **14**, 81: Ann. **446**, 49):

$$2R{\cdot}COOAg + I_2 \longrightarrow R{\cdot}COOR + CO_2 + 2AgI.$$

In the cold, complex compounds containing silver and iodine are formed (Constitution, see Ann. **446**, 52).

(6) Bromo-valeric acid, obtained from the fatty acid, gives up HBr to diethyl aniline or quinoline, becoming changed to ethylacrylic acid. This olefine monocarboxylic acid yields, on oxidation, propionic acid (C. 1899, I. 778):

$$\underset{\text{Valeric acid.}}{CH_3CH_2{\cdot}CH_2CH_2{\cdot}COOH} \longrightarrow \underset{\text{Ethylacrylic acid.}}{CH_3CH_2{\cdot}CH{=}CHCOOH} \longrightarrow \underset{\text{Propionic acid.}}{CH_3{\cdot}CH_2{\cdot}COOH.}$$

(7) α-Bromopelargonic acid, obtained from the unsubstituted acid, when

boiled with aqueous potassium hydroxide, yields α-hydroxypelargonic acid, which gives octyl aldehyde on being heated to 260° :

$$CH_3[CH_2]_7CH_2COOH \longrightarrow CH_3[CH_2]_7CHBrCOOH \longrightarrow$$
$$CH_3[CH_2]_7CH(OH)COOH \longrightarrow CH_3[CH_2]_7CHO.$$

(8) The dimethylnonylcarbinol obtained from capric acid by the action of magnesium methyl iodide, or the hydrocarbon obtained from the alcohol by loss of water, yield pelargonic acid when oxidized with permanganate (Compt. rend. **156**, 1443) :

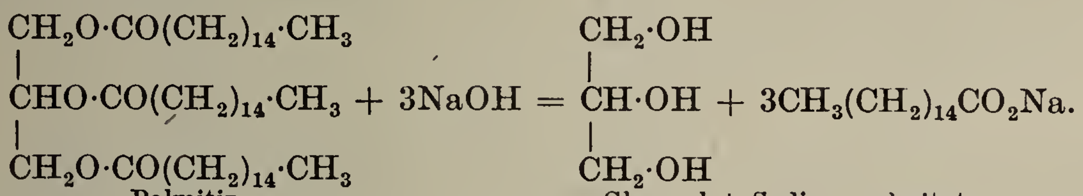
$$CH_3(CH_2)_7{\cdot}CH_2{\cdot}COOR \longrightarrow CH_3(CH_2)_7{\cdot}CH_2{\cdot}CMe_2OH \longrightarrow$$
$$CH_3(CH_2)_7{\cdot}CH : CMe_2 \longrightarrow CH_3(CH_2)_7{\cdot}COOH.$$

Technical Application of the Fats and Oils

Animal fats, especially mutton and beef-tallow, the nature of which was made clear by the classic researches of *Chevreul* in the beginning of last century, consist mainly of a mixture of glyceryl esters of palmitic, stearic, and oleic acids, which are commonly called *palmitin, stearin,* and *olein.* They are used in the preparation of *margarine,* in the manufacture of *stearin candles, soaps,* and *plasters,* from the acid esters contained in them, and for the manufacture of glycerol (*q.v.*). Palm oil, coconut oil, and olive oil are also used as raw material.

The so-called *stearin* of candles consists of a mixture of stearic and palmitic acids. For its preparation, beef-tallow and suet, both solid fats, are saponified with calcium hydroxide or sulphuric acid, with superheated steam, or by the action of ferments present in some seeds, such as castor-oil beans (Ber. **37**, 1436). The acids which separate are distilled with superheated steam. The yellow, semi-solid distillate, a mixture of stearic, palmitic, and oleic acids, is freed from the liquid oleic acid by pressing it between warm plates. The residual, solid mass is then melted together with some wax or paraffin, to prevent crystallization occurring when the mass is cold, and moulded into candles.

When the fats are saponified by potassium or sodium hydroxide, salts of the fatty acids—*soaps*—are produced, *e.g.* sodium palmitate, according to the equation :



$$\begin{array}{lcl} CH_2O{\cdot}CO(CH_2)_{14}{\cdot}CH_3 & & CH_2{\cdot}OH \\ | & & | \\ CHO{\cdot}CO(CH_2)_{14}{\cdot}CH_3 + 3NaOH & = & CH{\cdot}OH + 3CH_3(CH_2)_{14}CO_2Na. \\ | & & | \\ CH_2O{\cdot}CO(CH_2)_{14}{\cdot}CH_3 & & CH_2{\cdot}OH \end{array}$$

Palmitin. Glycerol + Sodium palmitate.

The sodium salts are solids and hard, whilst those of potassium are soft. Sodium chloride will convert potassium soaps into sodium soaps. In small quantities of water these salts of the alkalis dissolve completely, but with an excess of water they suffer hydrolytic dissociation into alkali and fatty acid. This is the cause of the emulsifying action of soap, whereby it is enabled to take up fatty materials, and so exercise its detergent action (Ber. **29**, 1328). The other metallic salts of the fatty acids are sparingly soluble or insoluble in water, but generally dissolve in alcohol. The lead salts, formed directly by boiling fats with litharge and water, constitute the so-called *lead plaster.*

Characterization of Fats.—*Saponification number.*—The amount of KOH used in the saponification of fats is a characteristic value for each fat. The number of milligrammes of KOH used in the saponification of 1 gm. fat is known as the saponification number.

Iodine Value.—Another characteristic of the natural fats is the amount of halogen (reckoned as iodine) they are capable of combining with. This depends, of course, on the quantity and nature of the unsaturated acids in the fat. The principal methods for its determination depend upon the use of a solution of iodine and mercuric chloride in alcohol (*Hübl*) or a solution of iodine monochloride in glacial acetic acid (*Wijs*).

Methods for the determination of the above, and the results for different fats are given in *Lewkowitsch*, Technology of Oils, Fats and Waxes, 6th edn., London, 1921.

The natural fats almost invariably contain a mixture of several fatty acids and unsaturated acids. When investigated carefully, natural glycerides are always found to contain more than one fatty acid (see Hilditch, Proc. Roy. Soc. [B] **103**, 113).

For the separation of the fatty acids in such a mixture, the following methods are used :

(1) Fractional precipitation with magnesium acetate (J. pr. Chem. **66**, 3).

(2) Fractional distillation of the acids in a high vacuum.

(3) Fractional distillation of the esters in a high vacuum (Z. angew. Chem. **24**, 1054).

FATTY ACID DERIVATIVES

1. ESTERS

The esters of the fatty acids have some similarity with the esters of the mineral acids (p. 159) and are prepared by similar methods.

Methods of Formation.—(1) By direct action of acids and alcohols, whereby water is formed at the same time :

$$C_2H_5{\cdot}OH + C_2H_3O{\cdot}OH = C_2H_5{\cdot}O{\cdot}C_2H_3O + H_2O.$$

This reaction, as already stated, only takes place slowly (p. 160) ; heat hastens it, but it is never complete. A detailed investigation into the formation of esters, which is of importance to the study of chemical dynamics, was carried out by Berthelot and Péan de St. Gilles.

If equivalent quantities of alcohol and acid be mixed, after a certain time a state of equilibrium will prevail between alcohol, acid, ester, and water ; if any further quantity of ester were formed it would be hydrolysed back to alcohol and acid by the water. In the case of acetic acid and ethyl alcohol, for example, this point is reached when about two-thirds of the acid has been esterified. If, however, an excess of alcohol is added to the mixture, the point of equilibrium is shifted in the direction of increased ester formation, so that a mixture of one equivalent of acetic acid and eight equivalents of alcohol is only in equilibrium when 0·945 equivalent of ester have been formed. The course of such a reaction is directed by the *Law of Mass Action*, developed by Guldberg and Waage (1867), and by van 't Hoff, which enunciates that the reaction between two bodies is dependent, not only on their affinity constant, but also on their relative concentrations.

In the case of esterification, if we designate as C_{acid} and C_{alc} the molar concentration of the acid and alcohol in the reacting mixture, then the velocity of the ester formation will be given by the equation:

$$v_1 = C_{acid} \cdot C_{alc} \cdot K_1,$$

where K_1 is a constant dependent on the nature of the reacting substances.

Similarly, the velocity of the reverse process, hydrolysis, is given by the equation:

$$v_2 = C_{ester} \cdot C_{water} \cdot K_2,$$

where C_{ester} and C_{water} represent the molar concentration of these substances and K_2 is another constant.

At equilibrium, the two reactions, esterification and hydrolysis, are proceeding at equal speeds, so that $v_1 = v_2$, or

$$C_{acid} \cdot C_{alc} \cdot K_1 = C_{ester} \cdot C_{water} \cdot K_2.$$

From this we deduce the equation:

$$\frac{C_{acid} \cdot C_{alc}}{C_{ester} \cdot C_{water}} = \frac{K_2}{K_1} = K,$$

or, expressed in words, the ratio of the product of the molar concentrations of the reactants to the product of the molar concentrations of the products, is at equilibrium, equal to the reciprocal of the ratio between the velocity constants.

From this equation, which is applicable to all bimolecular reactions where two substances A and B react to form two products C and D, it is readily seen that the process of esterification will proceed further if the ester or the water is removed from the reaction. Where the ester is readily volatile, this can be effected by distillation.

It is important to realize that while the attainment of equilibrium may be markedly hastened by the use of various catalysts, the position of such equilibrium is in no way altered. A collection of the various calculations applicable to such reactions is found in Ber. **17**, 2177 : **19**, 1700. Menschutkin has investigated the ester formation of various homologous series of acids and alcohols (Ann. **195**, 334 : **197**, 193 : Ber. **15**, 1445, 1572 : **21**, R. 41). It was found that the normal primary alcohols possessed the same velocity of reaction except methyl alcohol, which showed an increased value. The secondary alcohols entered more slowly into combination, and the tertiary slowest of all. Among the acids, formic acid exceeded that of acetic acid, and this in turn the homologues, in the initial velocity of esterification; apart from this they showed a diminishing velocity with increasing molecular complexity. Acids in which a primary alkyl group was contiguous to a carboxylic group, had a greater velocity than when a secondary alkyl group occupied that position, which in turn was greater than when a tertiary group was substituted.

From the practical point of view, direct esterification by the reaction between the acid and the alcohol is too slow, but by the addition of a strong mineral acid it can be markedly accelerated. The acceleration produced is proportional to the hydrogen ion concentration of the mixture.

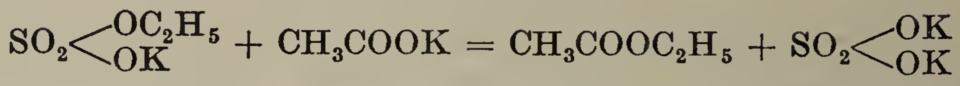
The process is therefore usually carried out in one of the following manners. (*a*) The acid or one of its salts is distilled with a mixture of the alcohol and sulphuric acid. This method is only applicable to the preparation of esters of low boiling point. (*b*) The acid is heated with five to ten times the quantity of about 5 per cent. alcoholic hydrochloric or sulphuric acid, for several hours, the excess alcohol distilled off, and the ester separated by dilution with water (Ber. **28**, 3201, 3215, 3252 : *cf.* Compt. rend. **156**, 1620). In the case of acids which esterify with difficulty, it is frequently desirable to dissolve the acid in excess alcohol and to saturate the solution with HCl gas (*cf.* Z. physikal. Chem. **66**, 275). (*c*) Another method of preparing esters consists in passing a mixture of the alcohol and acid over titanium oxide at 300° (Chem. Ztg. **37**, 777).

(2) Double decomposition of the alkyl esters of mineral acids with salts of the organic acids:

(*a*) By the action of the alkyl halides on salts of the acids, *e.g.* alkyl iodides and silver salts; or conveniently, the thallium salts (J.C.S. **1926**, 937):

$$C_2H_5I + CH_3COOAg = CH_3COOC_2H_5 + AgI.$$

(*b*) By the dry distillation of a mixture of the alkali salts of the fatty acids and salts of alkyl sulphates :



$$SO_2\left<\begin{matrix}OC_2H_5\\OK\end{matrix}\right. + CH_3COOK = CH_3COOC_2H_5 + SO_2\left<\begin{matrix}OK\\OK\end{matrix}\right.$$

(*c*) The methyl ester can be prepared from the sodium or potassium salt of the acid and dimethyl sulphate (Ber. **37,** 4144 : Ann. **340,** 244) :

$$2CH_3COOK + (CH_3)_2SO_4 = 2CH_3COOCH_3 + K_2SO_4.$$

(3*a*) By the action of acid chlorides (p. 314) or acid anhydrides (p. 317) on the alcohols or alcoholates ; and by the action of anhydrides or acid chlorides on alcohols in the presence of tertiary bases such as pyridine (Ber. **34,** 3554) :

$$C_2H_5OH + CH_3COCl = CH_3COOC_2H_5 + HCl.$$
$$C_2H_5OH + (CH_3CO)_2O = CH_3COOC_2H_5 + CH_3COOH.$$

In these reactions, it is sometimes more convenient to employ instead of the simple alcoholates, the halogen magnesium alcoholates ROMgX (prepared from alkyl magnesium halides and alcohols), on account of their solubility in ether (Ber. **39,** 1736).

(3*b*) By the action of acid chlorides on alkyl ethers in the presence of zinc chloride, *e.g.* ethyl ether and acetyl chloride yield chloroethane and ethyl acetate (Compt. rend. **132,** 1129).

(4) By the action of diazomethane on the acids (Ber. **31,** 501 : Monatsh. **22,** 229) :

$$R{\cdot}COOH + CH_2N_2 \xrightarrow{\qquad} R{\cdot}COOCH_3 + N_2.$$

(5) Acid nitriles are converted directly into esters when they are dissolved in alcohol and are subjected to the passage of HCl gas, or are heated with dilute acid (p. 326).

(6) Electro-syntheses of monocarboxylic esters, see p. 298.

(7) The fats, *i.e.* the glycerides of the fatty acids, are converted into the esters of the simple alcohols when heated with the alcohol in presence of hydrochloric acid (Compt. rend. **143,** 657 : **146,** 259).

Properties.—Usually, the esters of fatty acids are volatile, neutral liquids, soluble in alcohol and ether, but generally insoluble in water. Many of them possess an agreeable fruity odour, and are prepared in large quantities, as they find extended application as artificial fruit essences. Nearly all fruit-odours may be made by mixing the different esters. The esters of the higher fatty acids occur in the natural varieties of wax.

Consult Ber. **14,** 1274 : Ann. **218,** 337 : **220,** 290, 319 : **223,** 247, upon the boiling points, the specific gravities and specific volumes of the fatty acid esters.

Reactions.—(1) When the esters are heated with water they undergo a partial decomposition into alcohol and acid. This decomposition (*saponification* or *hydrolysis*) (p. 130) is more rapid and complete on heating with alkalis in alcoholic solution :

$$C_2H_3O{\cdot}OC_2H_5 + KOH = C_2H_3O{\cdot}OK + C_2H_5{\cdot}OH.$$

Consult Ann. **228,** 257, and **232,** 103 : Ber. **20,** 1634, upon the velocity of saponification by various bases.

(2) Ammonia changes the esters into amides (p. 321) :

$$C_2H_3O{\cdot}OC_2H_5 + NH_3 = C_2H_3O{\cdot}NH_2 + C_2H_5{\cdot}OH.$$

(3) The halogen acids convert the esters into acids and alkyl halides (Ann. **211**, 178):

$$C_2H_3O{\cdot}O{\cdot}C_2H_5 + HI = C_2H_3O{\cdot}OH + C_2H_5I.$$

This reaction enables the methoxy and ethoxy groups in esters to be estimated by Zeisel's method (see p. 11).

(4) By the action of PCl_5 the substituted hydroxyl oxygen is replaced by chlorine, and both radicals are converted into halogen derivatives. For the course of this reaction, see Oxalic ester.

$$C_2H_3O{\cdot}O{\cdot}C_2H_5 + PCl_5 = C_2H_3O{\cdot}Cl + C_2H_5Cl + POCl_3.$$

(5) The esters of the higher alcohols break down into fatty acids and olefines when heated or distilled under pressure. The same change takes place with the lower esters under the catalytic influence of the oxides of titanium, thorium, etc. (Chem. Ztg. **37**, 778).

(6) By reduction with sodium and absolute alcohol, the esters are reduced to the primary alcohol corresponding to the acid (C. 1905, II. 1700):

$$CH_3(CH_2)_4COOEt \longrightarrow CH_3(CH_2)_4CH_2OH.$$

(7) Potassium reacts with esters in absolute ethereal solution to form *enolates* (Ber. **53**, 388). Such enolates are very reactive compounds and play a part in the acetoacetic ester condensation (see p. 467):

$$2CH_3{\cdot}COOEt + 2K \longrightarrow 2CH_2 : C(OEt)(OK) + H_2.$$

The esters of **formic acid** have already been described (p. 283).

Esters of Acetic Acid.—The *methyl ester, methyl acetate*, $C_2H_3O_2{\cdot}CH_3$, b.p., 57·5°, $D_0 = 0{\cdot}9577$, occurs in crude wood-spirit. When chlorine acts on it the alcohol radical is first substituted: $C_2H_3O_2{\cdot}CH_2Cl$, b.p. 150°; $C_2H_3O_2{\cdot}CHCl_2$, b.p. 148°.

Ethyl ester, Ethyl acetate (loosely called acetic ether) (*Æther aceticus* of the B.P.), CH_3COOEt, b.p. 77°, m.p. − 82°, $D_0 = 0{\cdot}9238$. It is obtained technically from alcohol, acetic acid and sulphuric acid, or more recently from acetylene, via acetaldehyde, the ester being obtained from the aldehyde by the action of aluminium ethoxide (D.R.P. 308043, C. 1918, II. 693):

$$CH : CH \longrightarrow CH_3{\cdot}CHO \longrightarrow CH_3COOEt.$$

This method is also applicable to the preparation of higher esters (J.A.C.S., **45**, 3013: *cf.* D.R.P. 282660: C. 1915, I. 516).

It is a pleasant-smelling liquid, largely used as a solvent and for the preparation of acetoacetic ester. Chlorine produces substitution products by attacking the alkyl group.

n-*Propyl ester*, b.p. 101°; iso*Propyl ester*, b.p. 91°.

n-*Butyl ester*, b.p. 124°; iso*Butyl ester*, b.p. 116°; sec.-*Butyl ester*, b.p. 111°; tert.-*Butyl ester*, b.p. 96°; n-*Amyl ester*, b.p. 148°.

Methyl-n-*propylcarbinol acetate*, b.p. 133°. *Methyl*iso*propylcarbinol acetate*, b.p. 125°, is decomposed into amylene and acetic acid at 200°.

iso*Amyl acetate* (*acetic ester of fermentation amyl alcohol*), b.p. 140°, in dilute alcoholic solution possesses the odour of pears and is employed as "pear oil." It is used also in the varnish industry.

n-*Hexyl ester*, b.p. 169–170°, occurs in the oil of *Heracleum giganteum*, and possesses a fruit-like odour. n-*Octyl ester*, b.p. 207°, is also present in the oil of *Heracleum giganteum*, and has the odour of oranges.

Allyl ester, b.p. 98–100°.

For higher acetic esters, see Ann. **233**, 260.

The acetates of the hypothetical αα-glycols, $R{\cdot}CH(O{\cdot}COCH_3)_2$, have already been described in connection with the aldehydes (p. 244). The acetates of the polyhydric alcohols will be described later, under the alcohols from which they are derived.

Esters of Propionic Acid.—*Methyl ester*, b.p. 79·5° ; *Ethyl ester*, b.p. 98·8° ; n-*Propyl ester*, b.p. 122° ; iso*Butyl ester*, b.p. 137° ; iso*Amyl ester*, b.p. 160°, has an odour like that of pineapples (see Ann. **233**, 253).

Esters of *n*-Butyric Acid.—*Methyl ester*, b.p. 102·3°, has an odour like that of apples ; *ethyl ester*, b.p. 120·9°, has a pineapple-like odour, and is employed in the manufacture of artificial rum. Its alcoholic solution is the artificial *pineapple oil*,

n-*Propyl ester*, b.p. 143° ; iso*Propyl ester*, b.p. 128° ; iso*Butyl ester*, b.p. 157° ; iso*Amyl ester*, b.p. 178°, possesses an odour resembling that of pears ; n-*Hexyl ester*, b.p. 205° ; and n-*Octyl ester*, b.p. 244°, are found in the oil obtained from various species of *Heracleum* (see above) ; the octyl ester also occurs in *Pastinaca sativa* (Ann. **163**, 193 ; **166**, 80 ; **233**, 272).

Esters of *iso*Butyric Acid.—*Methyl ester*, b.p. 92·3° ; *Ethyl ester*, b.p. 110° ; n-*Propyl ester*, b.p. 135° (Ann. **218**, 334).

Esters of the Valeric Acids.—n-*Valeric ethyl ester*, b. p. 144°, (Ann. **233**, 274) ; iso-*Valeric ethyl ester*, b.p. 135° ; iso-*Valeric* iso*amyl ester*, b.p. 194°.

Methylethylacetic ethyl ester, b.p. 133·5° (Ann. **195**, 120) ; *Trimethylacetic ethyl ester*, b.p. 118° (Ann. **173**, 372).

Esters of the Hexoic Acids.—n-*Hexoic ethyl ester*, b.p. 167° ; iso*Butylacetic ethyl ester*, b.p. 161°.

***n*-Heptoic ethyl ester**, b.p. 187–188° ; n-*Octoic ethyl ester*, b.p. 207–208° (Ann. **233**, 282) ; n-*Nonoic ethyl ester*, b.p. 227–228° ; n-*Capric ethyl ester*, b.p. 243–245° ; n-*Capric* iso*amyl ester*, b.p. 275–290° (decomp.), is the principal constituent of the fusel oil of wine.

Lauric ethyl ester, b.p. 269° ; *Myristic ethyl ester*, m.p. 10–11°, b.p. 295°.

Spermaceti and the Waxes

Some of the esters with high molecular weights occur already formed in spermaceti and the waxes. This fact has been noted in connection with the corresponding alcohols and acids. The waxes are distinguished from the fats in that they consist of esters of monohydric alcohols with high molecular weight, whereas the fats are the esters of the trihydric alcohol, glycerol. Spermaceti belongs to the wax variety.

Spermaceti, *Cetaceum*, occurs in the oil from peculiar cavities in the heads of whales (particularly *Physeter macrocephalus*), and upon standing and cooling it separates as a white crystalline mass, which can be purified by pressing and recrystallization from alcohol. It consists of *cetyl palmitate*, $C_{16}H_{31}O_2{\cdot}C_{16}H_{33}$, m.p. 40°, which crystallizes from hot alcohol in waxy, shining needles or leaflets. It volatilizes undecomposed in a vacuum. Distilled under pressure, it yields hexadecylene and palmitic acid. When boiled with alcoholic potassium hydroxide it gives palmitic acid and cetyl alcohol (p. 149).

Waxes.—Ordinary *beeswax*, m.p. 61–64°, is a mixture of *cerotic acid*, $C_{26}H_{52}O_2$ or $C_{27}H_{54}O_2$, with *myricyl palmitate*, $C_{16}H_{31}O_2{\cdot}C_{30}H_{61}$. Boiling alcohol extracts the cerotic acid and the ester, *myricin*, remains (Ann. **224**, 225). Consult Ann. **235**, 106, for other constituents of beeswax.

Carnauba wax, m.p. 83°, occurs in the leaves of the carnauba tree, and contains free ceryl alcohol and various acid esters (Ann. **223**, 283).

Chinese wax or *Insect wax* is obtained by the *Coccus ceriferus*, Fabr., from the Chinese ash, *Fraxinus chinensis*. It consists mainly of *ceryl cerotate*, $C_{26}H_{51}O_2{\cdot}C_{26}H_{53}$, m.p. 81°. It is decomposed into cerotic acid and ceryl alcohol by alcoholic potassium hydroxide.

2. ACID HALIDES, OR HALOID ANHYDRIDES OF THE FATTY ACIDS

The acid halides (or haloid anhydrides of the acids) are the derivatives which arise in the replacement of the hydroxyl of acids by halogens ; they are the halogen compounds of the acid radicals. They have been termed haloid anhydrides, because they can be viewed as mixed anhydrides of the fatty acids and the halide acids, as shown by method of formation (1) of the acid chlorides.

Acid Chlorides.—*Formation.*—(1) From fatty acids and hydrochloric acid, by means of P_2O_5:

$$CH_3{\cdot}COOH + HCl \xrightarrow{P_2O_5} CH_3{\cdot}COCl + H_2O.$$

(2) By the action of hydrochloric acid gas on a mixture of an acid nitrile and a carboxylic acid or an anhydride at 0°. The hydrochloride of the acid amide is produced at the same time (Ber. **29**, R. 87):

$$CH_3CN + CH_3COOH + 2HCl = CH_3CONH_2{\cdot}HCl + CH_3COCl.$$

(3) By the action of chlorine on aldehydes:

$$CH_3COH + Cl_2 = CH_3COCl + HCl.$$

(4) A far more important method of formation consists in acting with phosphorus halides on the acids or their salts—just as the alkyl halides are produced from the alcohols (p. 161):

$$\begin{aligned} &(a) \quad CH_3COOH + PCl_5 = CH_3COCl + POCl_3 + HCl \\ &(b) \quad 3CH_3COOH + PCl_3 = 3CH_3COCl + H_3PO_3 \\ &(c) \quad 2CH_3COONa + POCl_3 = 2CH_3COCl + NaPO_3 + NaCl. \end{aligned}$$

In the presence of an excess of the salt, the anhydride of the acid is obtained instead of the expected acid chloride.

(5) Carbon oxychloride (Ber. **17**, 1285: **21**, 1267) and thionyl chloride (C. 1901, II. 527) react similarly to the phosphorus chlorides on free acids and their salts; as well as *p*-toluene sulphochloride or sodium chlorosulphonate, $NaOSO_2Cl$, on the salts (C. 1901, II. 518: 1904, I. 65) when acid chlorides and anhydrides are formed:

$$\begin{gathered} C_2H_3O{\cdot}OH + COCl_2 = C_2H_3OCl + HCl \\ CH_3COONa + NaOSO_2Cl = CH_3COCl + (NaO)_2SO_2. \end{gathered}$$

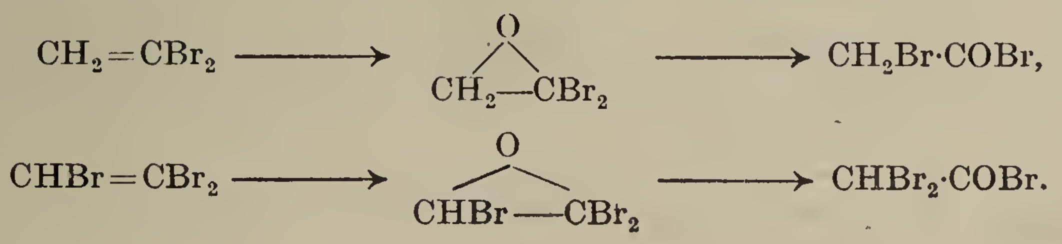
(6) Acid chlorides are also produced by the interaction of phosgene and zinc alkyls (p. 298).

Historical.—*Liebig* and *Wöhler* obtained the first acid chloride in 1832, when they treated benzaldehyde, C_6H_5COH, with chlorine and obtained benzoyl chloride, C_6H_5COCl, the chloride of the simplest aromatic acid—benzoic acid. In 1846, *Cahours* discovered the method of producing aromatic acid chlorides by the action of phosphorus pentachloride on monocarboxylic acids. Acetyl chloride was first prepared in 1851 by *Gerhardt* (Ann. **87**, 63) by treating sodium acetate with phosphorus oxychloride.

Acid Bromides.—(1) The phosphorus bromides act like the corresponding chlorides on the fatty acids or their salts. A mixture of amorphous phosphorus and bromine may be employed as a substitute for the bromide itself.

(2) The acid chlorides can be converted into the bromides by the action of excess of gaseous hydrogen bromide (Ber. **46**, 1417, 2162).

(3) An interesting method for preparing the bromides of brominated acetic acids consists in acting with air on certain bromide derivatives of ethylene, whereby oxygen is absorbed, and an intramolecular atomic rearrangement takes place. The reaction probably proceeds via the intermediate formation of an ethylene oxide (see p. 367 and Ber. **46**, 143: J. pr. Chem. [2], **85**, 78).



Acid Iodides.—Phosphorus iodide does not convert the acids into iodides of the acid radicals; this only occurs when the acid anhydrides are employed. They are also produced by the interaction of acid chlorides and hydriodic acid or calcium or magnesium iodides.

Acid Fluorides.—*Acetyl fluoride* is a gas with an odour resembling that of phosgene. It is formed in the action of AgF or AsF_3 on acetyl chloride. A better procedure consists in allowing acid chlorides to act on anhydrous zinc fluoride. *Propionyl fluoride*, $CH_3{\cdot}CH_2{\cdot}COF$, b.p. 44° (C. 1897, I. 1090).

Properties and Reactions.—The acid halides are sharp-smelling liquids, which fume in the air. They are heavier than water. (1) At ordinary temperatures in contact with water they decompose, forming carboxylic acids and halogen acids. The more readily soluble the resulting acid is in water, the more energetic will the reaction be.

The acid chlorides act similarly on many other bodies. (2) They yield esters, with the alcohols or alcoholates (p. 312). (3) With salts or acids they yield acid anhydrides (p. 317), and (4) with ammonia, the amides of the acids, etc. (p. 321). (5) Tertiary amines withdraw HCl from the acid chlorides, possibly with the intermediate formation of ketens, $R_2C{=}CO$, which undergo further change. Acetyl chloride yields dehydracetic acid, $C_8H_8O_4$ (*q.v.*); *iso*butyryl chloride gives tetramethyldiketo*cyclo*butane $[(CH_3)_2C{\cdot}CO]_2$ (Vol. II) (Ber. **39**, 1631).

(6) Sodium amalgam, or better, sodium and oxalic acid (Ber. **2**, 98), will convert the acid chlorides into aldehydes (p. 226), which can be further reduced to primary alcohols (p. 131). In the presence of "sulphured quinoline" the reduction to aldehydes can be carried out catalytically by hydrogen and palladium (Ber. **51**, 585: **54**, 2888: **55**, 609).

(7) They yield ketones and tertiary alcohols when treated with the zinc alkyls (pp. 257, 132). (8) By the action of silver cyanide they pass into the acyl cyanides, which are described as the nitriles of the α-ketone carboxylic acids. (9) Di- and poly-carboxylic acids, having the power of forming anhydrides, are converted into their anhydrides when treated with acid chlorides.

(10) The acid chlorides react with diazomethane with the primary formation of a diazoketone:

$$R{\cdot}COCl + CH_2N_2 \longrightarrow R{\cdot}CO{\cdot}CHN_2 + HCl.$$

Under certain circumstances a chloro-ketone is formed by the action of the halogen acid on the diazo compound (J.C.S. **1928**, 1310, 2904: see, however, J.C.S. **117**, 1153: J.A.C.S. **46**, 2554: Ber. **60**, 1026, where the primary formation of a chloroketone is postulated).

Acetyl chloride, *Ethanoyl chloride*, $CH_3{\cdot}CO{\cdot}Cl$, b.p. 55°, $D_0 = 1{\cdot}130$, is formed according to the general methods applied in the production of acid chlorides, and is prepared by carefully distilling a mixture of acetic acid (3 parts) and PCl_3 (2 parts), or, by heating $POCl_3$ (2 molecules) with acetic acid (3 molecules), as long as HCl escapes, and then distilling (Ann. **175**, 378). The acetyl chloride is purified by a second distillation, this time over a little dry sodium acetate.

It is a colourless pungent-smelling liquid, rapidly decomposed by water, with formation of acetic acid. Chlorine reacts with acetyl chloride to form the chlorides of the chlorinated acetic acids. It reacts with aluminium chloride to produce acetylacetone (*q.v.*).

Acetyl bromide, b.p. 81°. *Acetyl iodide*, b.p. 108°.

Propionyl chloride, $CH_3{\cdot}CH_2COCl$, b.p. 80°; *bromide*, b.p. 104°; *iodide*, b.p. 127°.

Butyryl chloride, C_4H_7OCl, b.p. 101° (Ber. **34**, 4051). Aluminium chloride changes it to triethyl phloroglucinol (Ber. **27**, R. 507; *bromide*, b.p. 128°; n-*iodide*, b.p. 146°; *iso***Butyryl chloride,** $(CH_3)_2CH{\cdot}COCl$, b.p. 92°; *bromide*, b.p. 116°.

Valeryl chloride, b.p. 127°; *iso***Valeryl chloride,** C_5H_9OCl, b.p. 114·5°; *bromide*, b.p. 143°; *iodide*, b.p. 168°. **Trimethylacetyl chloride,** b.p. 105–106°.

n-Caproyl chloride, $CH_3(CH_2)_4COCl$, b.p. 146°; **Diethylacetyl chloride,** $(C_2H_5)_2CHCOCl$, b.p. 135°; **Dimethylethylacetyl chloride,** $(CH_3)_2(C_2H_5)C{\cdot}COCl$, b.p. 132°.

Consult Ber. **17**, 1378: **19**, 2982: **23**, 2384, for the chlorides of the higher fatty acids.

The boiling point of the normal acid chlorides shows an increase of 48° between each member of the series and its next but one higher member. This interval is made up of 28° between a chloride containing an even number of carbon atoms and the next higher member, which, of course, contains an odd number, and 20° between this and the next higher which possesses an even number of carbon atoms (C. 1899, I. 968).

Mixed Anhydrides with Inorganic Oxyacids

The mixed anhydrides of a fatty acid with the various inorganic oxyacids can be conveniently dealt with in this section.

Acetylsulphuric acid, $CH_3{\cdot}CO{\cdot}O{\cdot}SO_3H$.—This compound is formed when sulphur trioxide acts on acetic acid below 0°. On heating to 70°, sulphoacetic acid, $SO_3H{\cdot}CH_2{\cdot}COOH$, is the principal product. It acts as a vigorous acetylating agent, such substances as tribromophenol being readily acetylated. Under suitable conditions it acts as a sulphonating agent, and benzene is sulphonated to benzenesulphonic acid (*van Peski*, Rec. Trav. Chim. **40**, 103).

Diacetyl orthonitric acid, $(CH_3COO)_2N(OH)_3$, b.p. 128°, $D_{15}=1{\cdot}197$, results when nitric acid (D. = 1·4) reacts with acetic anhydride, or glacial acetic acid with fuming nitric acid. It is a colourless liquid, fuming in air, and decomposed by water into acetic and nitric acids. It possesses an oxidizing and nitrating action. Excess of acetic anhydride converts it into tetranitromethane, $C(NO_2)_4$ (Ber. **35**, 2526; **36**, 2225).

Acetyl nitrite, $CH_3COO{\cdot}NO_2$, b.p. 22°/77 mm., is prepared from N_2O_5 and acetic anhydride. It is a colourless mobile liquid, fuming in air, and explodes when rapidly heated. At 60° it evolves nitrous fumes and forms tetranitromethane. With alcohol it forms a mixture of acetic and nitric esters. It is strong nitrating mixture for benzene derivatives (C. 1907, I. 1025).

Acetyl nitrite, $CH_3COO{\cdot}NO$, is obtained from silver acetate and NOCl, and forms an easily decomposed golden-yellow liquid (C. 1904, II. 511).

Acetyl chromate, $(CH_3COO)CrO_3H$, results from mixing CrO_3 and glacial acetic acid (Ber. **36**, 2215).

Triacetyl borate, m.p. 121°, is obtained from B_2O_3 and acetic anhydride. Alcohols produce from it boric ester, whilst carboxylic acids give rise to other mixed boric anhydrides, such as *tristearyl borate*, $(C_{18}H_{35}O_2)B$, m.p. 71° (Ber. **36**, 2219).

Acetyl arsenite, m.p. 82°, b.p. 165-170°/31 mm., is formed from As_2O_3 and acetic anhydride (C. 1906, I. 21).

3. CARBOXYLIC ACID ANHYDRIDES, ACYL OXIDES

The acid anhydrides are the oxides of the acid radicals. In those of the monobasic acids two acid radicals are united by an oxygen atom; they are analogous to the oxides of the univalent alcohol radicals—the ethers.

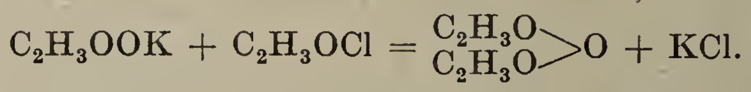
The *simple* anhydrides, containing two similar radicals, can usually be distilled, whilst the *mixed* anhydrides, with two dissimilar radicals, decompose when heated, into two simple anhydrides:

$$2\left.\begin{matrix}C_2H_3O\\C_5H_9O\end{matrix}\right>O = \left.\begin{matrix}C_2H_3O\\C_2H_3O\end{matrix}\right>O + \left.\begin{matrix}C_5H_9O\\C_5H_9O\end{matrix}\right>O.$$

Hence they cannot be separated from the product of the reaction by distillation, but have to be dissolved out with ether.

Formyl acetyl oxide, $HCO{\cdot}O{\cdot}COCH_3$, however, can be volatilized unchanged under reduced pressure.

Methods of Formation.—(1*a*) The chlorides of the acid radical are allowed to act on anhydrous salts, such as the alkali salts of the acids :



$$C_2H_3OOK + C_2H_3OCl = \begin{matrix}C_2H_3O\\C_2H_3O\end{matrix}\!\!>O + KCl.$$

(1*b*) The anhydrides of the higher fatty acids can also be produced by the action of acetyl chloride (Ber. **10,** 1881 : Bull. Soc. Chim. [4] **5,** 920) or acetic anhydride (Ann. **226,** 12 : C. 1899, I. 1070) on the free acids ; in the latter case mixed anhydrides are also obtained. The action of the chloride on the free carboxylic acids is assisted by the presence of a tertiary base, such as pyridine, quinoline, or triethylamine, which takes up the hydrochloric acid set free during reaction (Ber. **34,** 2070 : C. 1901, II. 543).

(2) Phosphorus oxychloride (1 molecule) acts on the dry alkali salts of the acids (4 molecules). The acid chloride, which is first produced, reacts immediately on its formation with the excess of salt :

$$\text{I.}\quad 2C_2H_3O{\cdot}OK + POCl_3 = 2C_2H_3O{\cdot}Cl + KPO_3 + KCl$$
$$\text{II.}\quad C_2H_3O{\cdot}OK + C_2H_3O{\cdot}Cl = (C_2H_3O)_2O + KCl.$$

(3) Phosgene, $COCl_2$, acts like $POCl_3$. In this reaction acid chlorides are also produced (p. 315).

(4) A direct conversion of the acid chlorides into the corresponding anhydrides may be effected by the action of the former on anhydrous oxalic acid (Ann. **226,** 14) :

$$2C_2H_3OCl + C_2O_4H_2 = (C_2H_3O)_2O + 2HCl + CO_2 + CO.$$

Historical.—Gerhardt (1851) discovered the acid anhydrides. The important bearing of this discovery upon the type theory has already been alluded to in the Introduction.

Properties and Reactions.—The acid anhydrides are liquids or solids of neutral reaction, and are soluble in ether. Their boiling points are higher than those of the corresponding acids.

(1) Water decomposes them into their constituent acids :

$$(CH_3CO)_2O + H_2O = 2CH_3COOH.$$

(2) With alcohols they yield the esters (C. 1906, II. 1043) :

$$(CH_3CO)_2O + C_2H_5OH = CH_3COOC_2H_5 + CH_3COOH.$$

(3) Ammonia and primary and secondary amines convert them into amides and ammonium salts :

$$(CH_3CO)_2O + 2NH_3 = CH_3CONH_2 + CH_3COONH_4.$$

(4) Heated with hydrochloric acid, hydrobromic and hydriodic acids, they decompose into an acid halide and free acid :

$$(CH_3CO)_2O + HCl = CH_3COCl + CH_3COOH.$$

(5) Chlorine splits them up into acid chlorides and chlorinated acids :

$$(CH_3CO)_2O + Cl_2 = CH_3COCl + ClCH_2COOH.$$

(6) Sodium amalgam changes the anhydrides to aldehydes and primary alcohols.

(7) Aldehydes and acid anhydrides combine to form alkylidene diacetates (Ann. **402**, 115).

Simple Anhydrides.—*Acetic anhydride*, $(CH_3{\cdot}CO)_2O$, is a mobile pungent liquid, b.p. 139°, $D^{20}_4 = 1{\cdot}0820$ (J.C.S. **101**, 1720). It is decomposed by a heated platinum spiral dipping into the liquid with formation of keten (p. 270).

It is prepared by distillation of a mixture of anhydrous sodium acetate (three parts) and $POCl_3$ (one part); or of the product of reaction of equal parts of acetyl chloride and sodium acetate. The anhydride can be dissolved undecomposed in about ten parts of cold water, and in this form may be used for acetylating amino-bases in aqueous solution (C. 1905, II. 466; 1906, II. 1042).

Propionic anhydride, $(C_3H_5)_2O$, b.p. 168°. *Butyric anhydride*, b.p. 199°. iso*Butyric anhydride*, b.p. 181·5°. n-*Caproic anhydride*, b.p. 242°, with decomposition. *Œnanthic anhydride*, m.p. 17°, b.p. 164°/15 mm. n-*Octylic anhydride*, m.p. − 1°, b.p. 186°/15 mm. *Pelargonic anhydride*, m.p. 16°, b.p. 207°/15 mm. *Palmitic anhydride*, m.p. 64°. *Stearic anhydride*, m.p. 72° (C. 1899, I. 1070: Ber. **33**, 3576).

Further anhydrides, see Ber. **58**, 1418.

Mixed Anhydrides.—*Acetyl formyl oxide*, $HCO{\cdot}O{\cdot}COCH_3$, b.p. 29°/18 mm., is prepared by mixing formic acid and acetic anhydride in the cold, a reaction which can be employed for the formation of higher homologues. At ordinary pressures it boils with partial decomposition. Quinoline liberates CO, and alcohols form formyl esters (C. 1900, II. 750). For other mixed anhydrides, see Ber. **34**, 168.

4. PER-ACIDS AND ACYL PEROXIDES

The per-acids (hydroperoxides), $R{\cdot}COO_2H$, and the acyl peroxides, $(R{\cdot}CO)_2O_2$, can be regarded as derivatives of hydrogen peroxide in which one or two hydrogen atoms have been replaced by acyl groups.

The **per-acids** are formed by the action of pure hydrogen peroxide on the acids or acid anhydrides in presence of a little strong sulphuric acid (*d'Ans*, Ber. **45**, 1845: Z. anorg. Chem. **84**, 145):

$$CH_3COOH + H_2O_2 \longrightarrow CH_3COO_2H + H_2O$$
$$(CH_3CO)_2H + H_2O_2 \longrightarrow CH_3COO_2H + CH_3COOH.$$

The per-acids are the primary autoxidation products of the aldehydes (D.R.P. 269937: C. 1914, I. 716).

Peracetic acid (*Acetyl hydroperoxide*), CH_3COO_2H, m.p. 0·1°, is a clear, pungent-smelling liquid. It explodes violently on heating. It is most readily obtained by the action of H_2O_2 on acetic-boric anhydride (p. 317) *Perpropionic acid* (*Propionyl hydroperoxide*), b.p. 25°/20 mm., m.p. −13·5°.

The **peroxides** of the acid radicals are prepared by heating the chlorides or anhydrides in ethereal solution with barium peroxide (*Brodie*, Pogg. Ann. **121**, 382), or by the action of the ice-cold chloride on sodium peroxide hydrate (Ber. **33**, 1043):

$$(C_2H_3O)_2O + BaO_2 = (C_2H_3O)_2O_2 + BaO.$$

Diacetyl peroxide, m.p. 30°, b.p. 63°/21 mm., possesses a sharp odour like ozone. It is insoluble in water, but easily soluble in alcohol and ether. It is very unstable and acts as a strong oxidizing agent, liberating iodine from a KI solution, and decolorizing a solution of indigo. Sunlight decomposes it, and it explodes violently on heating. *Propionic peroxide*, $(C_3H_5O)_2O_2$, is obtained from propionic anhydride and BaO_2: it is a liquid (C. 1903, I. 958).

Reactions of the peroxides: see Ber. **59**, 662.

5. THIO-ACIDS

By the replacement of oxygen in the carboxyl group by sulphur, the thio-acids are formed.

(1) The **monothio acids**, which in the free condition probably have the constitution $R{\cdot}CO{\cdot}SH$ (see Ber. **46**, 3581), form derivatives both of this form (*carbothiolic acids*) and also of the tautomeric form, $R{\cdot}CS{\cdot}OH$ (*carbothionic acids*).

Thioacetic acid, $CH_3{\cdot}COSH$, was obtained by *Kekulé* (Ann. **90**, 309) when phosphorus pentasulphide acted on acetic acid. In its preparation it is advisable to mix the P_2S_5 with half its weight of coarse fragments of glass:

$$5C_2H_3O{\cdot}OH + P_2S_5 = 5C_2H_3O{\cdot}SH + P_2O_5.$$

The *thio-anhydrides* arise in the same manner by the action of phosphorus sulphide on the acid anhydrides. The thio-acids are produced by the action of acid chlorides on potassium hydrogen sulphide, or from phenyl esters and NaSH in alcoholic solution (C. 1903, I. 816).

Thioacetic acid, *methanecarbothiolic acid,* CH_3COSH, b.p. 93°, $D_{10} = 1{\cdot}074$, is a colourless liquid. Its odour resembles those of acetic acid and hydrogen sulphide. It dissolves with difficulty in water, but readily in alcohol and in ether. This acid has been recommended as a very convenient substitute for hydrogen sulphide in analytical operations (C. 1901, I. 1148) and is a suitable reagent for acetylating amines (Ber. **35**, 110). The *lead salt,* $(C_2H_3O{\cdot}S)_2Pb$, crystallizes in minute needles, and readily decomposes with the formation of lead sulphide (C. 1897, I. 1090: II. 770).

When thioacetic acid is heated with zinc chloride, there is formed *tetraethenyl hexasulphide,* $(CH_3C)_4S_6$, m.p. 224° (Ber. **36**, 204).

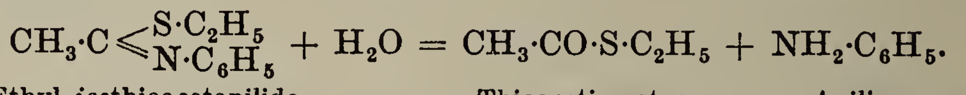
Thiopropionic acid, *ethanecarbothiolic acid,* C_2H_5COSH, from ethyl magnesium bromide and carbon oxysulphide, see Ber. **36**, 1009.

Acetyl sulphide, $(C_2H_3O)_2S$, b.p. 157°, is a heavy yellow oil, insoluble in water. Water gradually decomposes it into acetic and thioacetic acids (Ber. **24**, 3548, 4251).

Acetyl disulphide, $(C_2H_3O)_2S_2$, is formed when acetyl chloride acts on potassium disulphide, or iodine on the salts of the thio-acid.

The *S*-**esters** are obtained when the alkylhalides react with the salts of the thio-acids, and the acid chlorides with the mercaptans or mercaptides.

They also appear in the decomposition of alkyl *iso*thioacetanilides with dilute hydrochloric acid:



$$CH_3{\cdot}C{\lessdot}^{S\cdot C_2H_5}_{N\cdot C_6H_5} + H_2O = CH_3{\cdot}CO{\cdot}S{\cdot}C_2H_5 + NH_2{\cdot}C_6H_5.$$

Ethyl *iso*thioacetanilide. Thioacetic ester. Aniline.

Concentrated potassium hydroxide decomposes the esters into fatty acids and mercaptans.

Thioacetic S-*ethyl ester,* $CH_3{\cdot}CO{\cdot}SEt$, b.p. 115°.

The *O*-**esters** are obtained by the action of magnesium alkyl halides on the *O*-esters of chlorothioformic acid (Compt. rend. **153**, 279):

$$Cl{\cdot}CS{\cdot}OEt + MgMeI \longrightarrow Me{\cdot}CS{\cdot}OEt + MgClI$$

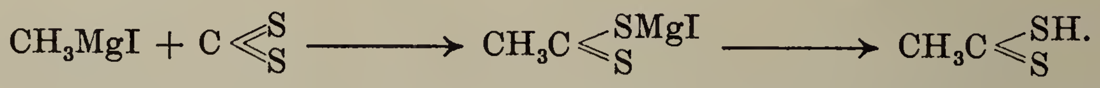
or by the action of hydrogen sulphide on imidoethers (C. 1909, II. 423):

$$CH_3{\cdot}C(:NH){\cdot}OEt + H_2S \longrightarrow CH_3{\cdot}CS{\cdot}OEt + NH_3.$$

Thioacetic acid O-*ethyl ester,* $CH_3{\cdot}CS{\cdot}OEt$, b.p. 109°, is a bright yellow oil with an unpleasant odour. *Thiopropionic acid* O-*ethyl ester,* b.p. 131°.

(Under certain circumstances, the alkyl group may migrate from oxygen to sulphur: see phenyl thiocarbonate, Ber. **63**, 178).

(2) **Dithio Acids** (*Carbodithioic acids*).—Just as carboxylic acids result from the treatment of acetyl magnesium halides with CO_2, so the doubly sulphur-substituted carboxylic acids are prepared by the action of CS_2 on the alkyl magnesium halides:



$$CH_3MgI + C{\lessdot}^{S}_{S} \longrightarrow CH_3C{\lessdot}^{SMgI}_{S} \longrightarrow CH_3C{\lessdot}^{SH.}_{S}$$

They are reddish-yellow oils, of an offensive odour, which can be distilled without decomposition. They are strong acids, easily oxidized in the air to solid, stable, yellow disulphides, $RCSS{\cdot}SCSR$.

Methanecarbodithioic acid, CH_3CS_2H, b.p. 37°/15 mm., $D_{20} = 1{\cdot}24$, is prepared from methyl magnesium iodide and CS_2. It is a reddish-yellow oil, of an exceedingly penetrating and repulsive odour; it dissolves with difficulty in water, but easily in organic solvents. *Ethanecarbodithioic acid,* $C_2H_5CS_2H$, b.p. 48°/17 mm. *Propanecarbodithioic acid,* b.p. 59°/13 mm. iso*Butanecarbodithioic acid,* b.p. 84°/33mm. iso*Pentanecarbodithioic acid,* b.p. 84°/10 mm. (Ber. **40**, 1725: **44**, 3226).

6. ACID AMIDES

These correspond with the amines of the alcohol radicals. The hydrogen of ammonia can be replaced by acid radicals, forming primary, secondary and tertiary acid amides:

$CH_3CO{\cdot}NH_2$	$(CH_3CO)_2NH$	$(CH_3CO)_3N$
Acetamide (primary).	Diacetamide (secondary).	Triacetamide (tertiary).

The primary acid amides have as isomers, the imido-ethers (p. 328) of the formula $R'{\cdot}C{<}\genfrac{}{}{0pt}{}{OH}{NH}$. To benzamide (Vol. II) is ascribed, not only the formula $C_6H_5C{<}\genfrac{}{}{0pt}{}{O}{NH_2}$, but also $C_6H_5C{<}\genfrac{}{}{0pt}{}{OH}{NH}$, since the silver derivative and iodoethane give benzimido-ethyl ether, $C_6H_5C{<}\genfrac{}{}{0pt}{}{OC_2H_5}{NH}$. The sodium derivative is the only one which, on reacting with iodoethane, gives a benzamide in which the imide group is ethylated (C. 1900, I. 1070: Ber. **34**, 1614). The constitution of the free amide cannot be deduced from the reactions of its metallic derivatives any more than that of acetoacetic ester can be deduced from the reactions of its sodium derivative.

The hydrogen of primary and secondary amines, like that of ammonia, can be replaced by acid residues, giving rise to substituted amides.

General Methods of Formation.—(1) By the dry distillation of the ammonium salts of the acids of this series. A better yield is obtained by merely heating the ammonium salts to about 230° (Ber. **15**, 979) (*Kündig*, 1858). (This method was first applied (1830) by Dumas to ammonium oxalate with the production of oxamide):

$$\underset{\text{Ammonium acetate.}}{CH_3CO{\cdot}ONH_4} = \underset{\text{Acetamide.}}{CH_3CONH_2} + H_2O.$$

A mixture of the sodium salts and ammonium chloride may be substituted for the ammonium salts. Consult Ber. **17**, 848, upon the velocity and limit of the amide production.

(2) By the action of ammonia, primary and secondary amines on the esters whereby Liebig, in 1834, obtained oxamide from oxalic ester:

$$CH_3CO{\cdot}O{\cdot}C_2H_5 + NH_3 = \underset{\text{Acetamide.}}{CH_3CO{\cdot}NH_2} + C_2H_5{\cdot}OH$$

$$CH_3CO{\cdot}O{\cdot}C_2H_5 + C_2H_5{\cdot}NH_2 = \underset{\text{Acetethylamide.}}{CH_3CONHC_2H_5} + C_2H_5{\cdot}OH.$$

This reaction takes place in the cold, particularly in the case of water-soluble esters; or the ester may be heated with an aqueous or alcoholic solution of ammonia.

It is one of the so-called reversible reactions, inasmuch as the action of alcohols on acid amides again produces esters and ammonia (Ber. **22**, 24).

(3) By the action (*a*) of acid halides, (*b*) of acid anhydrides on ammonia, primary and secondary alkylamines. This was the method which Liebig and Wöhler first used in 1832 to prepare benzamide from benzoyl chloride.

(3*a*) $$CH_3COCl + 2NH_3 = \underset{\text{Acetamide.}}{CH_3CONH_2} + NH_4Cl$$

$$CH_3COCl + 2NH_2C_2H_5 = \underset{\text{Acetethylamide.}}{CH_3CONH{\cdot}C_2H_5} + N(C_2H_5)H_3Cl$$

$$CH_3COCl + 2NH(C_2H_5)_2 = \underset{\text{Acetdiethylamide.}}{CH_3CON(C_2H_5)_2} + N(C_2H_5)_2H_2Cl.$$

This method is especially well adapted for obtaining the amides of the higher fatty acids (Ber. **15**, 1728):

(3*b*) $(CH_3CO)_2O + 2NH_3 = CH_3CONH_2 + CH_3{\cdot}CO_2NH_4$
$(CH_3CO)_2O + 2NH_2C_2H_5 = CH_3CONHC_2H_5 + CH_3CO_2NH_3C_2H_5.$

(4) By the addition of one molecule of water to the nitriles of the acids (p. 324):

$$\underset{\text{Acetonitrile.}}{CH_3CN} + H_2O\ (180°) = \underset{\text{Acetamide.}}{CH_3CONH_2}.$$

This addition of water frequently occurs in the cold by the action of concentrated hydrochloric acid, or by mixing the nitrile with glacial acetic acid and concentrated sulphuric acid (Ber. **10**, 1061). Hydrogen peroxide in alkaline solution also converts the nitriles, with liberation of oxygen, into amides (Ber. **18**, 355). For the action of hydrochloric acid on a mixture of nitrile and fatty acid see (2), formation of acid chlorides.

(5) By the distillation of the fatty acids with potassium thiocyanate:

$$2C_2H_3O{\cdot}OH + KSNC = C_2H_3O{\cdot}NH_2 + C_2H_3O{\cdot}OK + COS.$$

Simply heating the mixture is more practical (Ber. **15**, 978; **16**, 2291). In making acetamide, glacial acetic acid and ammonium thiocyanate are heated together for several days. By this reaction the aromatic acids yield nitriles.

(6) By the interaction of fatty acids and carbylamines (p. 293):

$$2CH_3COOH + C:N{\cdot}CH_3 = \underset{\text{Methylformamide.}}{HCONHCH_3} + (CH_3CO)_2O.$$

(7) By the action of the fatty acids on *iso*cyanic esters (*q.v.*):

$$CH_3COOH + CON{\cdot}C_2H_5 = CH_3{\cdot}CONHC_2H_5 + CO_2.$$

Secondary and **tertiary amides** are obtained (1) by heating primary acid amides (Ber. **23**, 2394), alkyl cyanides or nitriles with acids, or acid anhydrides, to 200°.

$$CH_3CONH_2 + (CH_3CO)_2O = (CH_3CO)_2NH + CH_3COOH$$
$$CH_3CN + CH_3COOH = \underset{\text{Diacetamide.}}{(CH_3CO)_2NH}$$
$$CH_3CN + (CH_3CO)_2O = \underset{\text{Triacetamide.}}{(CH_3CO)_3N}.$$

Diacetamide is also prepared by the action of acetyl chloride on acetamide in solution in benzene (C. 1901, I. 678).

(2) The secondary amides can also be prepared by heating primary amides with dry hydrogen chloride:

$$2C_2H_3ONH_2 + HCl = \underset{\text{Diacetamide.}}{(C_2H_3O)_2NH} + NH_4Cl.$$

(3) Secondary amides are formed by heating acid anhydrides with potassium cyanate (Ber. **47**, 267).

(4) Substituted secondary amides are further produced by the action of esters of *iso*cyanic acid on acid anhydrides:

$$(C_2H_3O)_2O + CO:N{\cdot}C_2H_5 = \underset{\text{Diacetethylamide.}}{(C_2H_3O)_2N{\cdot}C_2H_5} + CO_2.$$

Properties and Reactions.—The amides of the fatty acids are usually solid, crystalline bodies, soluble in both alcohol and ether. The lower members are also soluble in water, and can be distilled without decomposition. As they contain the basic amido-group they are able to unite directly with acids, forming salt-like derivatives, *e.g.*

$C_2H_3ONH_2{\cdot}HNO_3$ and $(CH_3CONH_2)_2{\cdot}HCl$, but these are not very stable, because the basic character of the amido-group is greatly weakened by the acid radical. Furthermore, the acid radical imparts to the NH_2-group the power of exchanging a hydrogen atom for metals, such as mercury or sodium (Ber. **23**, 3037 : C. 1902, II. 787), forming metallic derivatives, *e.g.* $(CH_3{\cdot}CO{\cdot}NH)_2{\cdot}Hg$—mercury acetamide, analogous to the salts of the imides of dibasic acids.

Reactions.—(1) The C·N linkage in the amides is very much more easily broken than that in the amines, and the amides readily take up water with the formation of the ammonium salts, or the acids and ammonia. Heating with water effects this, although it is more easily accomplished by boiling with alkalis or acids. This reaction is termed hydrolysis.

$$CH_3CO{\cdot}NH_2 + H_2O = CH_3CO{\cdot}OH + NH_3.$$

(2) Nitrous acid decomposes the primary amides similarly to the primary amines (p. 194), with the formation of a carboxylic acid and nitrogen.

$$C_2H_3O{\cdot}NH_2 + HNO_2 = C_2H_3O{\cdot}OH + N_2 + H_2O.$$

Acid amides, which hydrolyse with difficulty, may be dissolved in concentrated sulphuric acid, to which sodium nitrite is added in the cold (Ber. **28**, 2783).

(3) Bromine in alkaline solution changes the primary amides to bromoamides (Ber. **15**, 407 and 752) :

$$C_2H_3O{\cdot}NH_2 + Br_2 = C_2H_3O{\cdot}NHBr + HBr,$$

which then form amines (p. 191).

(4) On heating with phosphorus pentoxide or chloride, they part with one molecule of water and become converted into nitriles (cyanides of the alcohol radicals) :

$$CH_3{\cdot}CO{\cdot}NH_2 = CH_3{\cdot}CN + H_2O.$$

With PCl_5 the replacement of an oxygen atom by two chlorine atoms takes place ; the resulting chlorides, like $CH_3{\cdot}CCl_2{\cdot}NH_2$, then lose, upon further heating, two molecules of HCl with the formation of nitriles.

(5) The acid amides condense with chloral to compounds of the type $CCl_3CH(OH){\cdot}CH{\cdot}COR$, which by the action of acetic anhydride and alkali yield anhydro derivatives with an ether linkage, of the general formula $R{\cdot}CO{\cdot}NH{\cdot}CH(CCl_3){\cdot}O{\cdot}CH(CCl_3){\cdot}NH{\cdot}CO{\cdot}R$ (Ber. **45**, 945 : **47**, 1173).

Formamide, $H{\cdot}CONH_2$. See p. 284.

Acetamide [Ethanamide], $CH_3CO{\cdot}NH_2$, m.p. 82°, b.p. 222°, crystallizes in long needles. It dissolves with ease in water and alcohol. In explaining the methods of producing the amides, and in illustrating their behaviour, acetamide was presented as the example. Dumas, Leblanc, and Malaguti first prepared it in 1847, by allowing ammonia to act on acetic ester. For the preparation of acetamide from ammonium acetate, see C. 1906, I. 1089 : J.A.C.S. **35**, 1780.

Acetomethylamide, $CH_3{\cdot}CONHCH_3$, m.p. 28°, b.p. 206° ; *Acetodimethylamide*, $CH_3{\cdot}CO{\cdot}N(CH_3)_2$ b.p. 165·5° ; *Acetethylamide*, b.p. 205° ; *Acetodiethylamide*, b.p. 185–186°. *Methylene diacetamide*, $CH_2(NHCOCH_3)_2$, m.p. 196°, b.p. 288° (Ber. **25**, 310).

Chloralacetamide, $CCl_3CH(OH)NHCOCH_3$, m.p. 158° (Ber. **10**, 168). *Anhydrochloral acetamide*, $[CH_3{\cdot}CO{\cdot}NH{\cdot}CH(CCl_3)]_2O$, m.p. 213° (Ber. **45**, 957).

Acetamide and butyl chloral yield two isomeric compounds, m.p. 158° and 170° respectively (Ber. **25**, 1690).

Diacetamide, $(C_2H_3O)_2NH$, m.p. 77°, b.p. 222·5–223·5°, is readily soluble in water. (Preparation, p. 322). *Diacetmethylamide* $(CH_3CO)_2N\cdot CH_3$, b.p. 192°. *Diacetethylamide,* b.p. 185–192°.

Triacetamide, $(C_2H_3O)_3N$, m.p. 78–79°. (Preparation, p. 322).

Acetochloroamide, $CH_3CONHCl$, m.p. 110°. *Acetobromoamide,* $CH_3CONHBr + H_2O$, forms large plates, and melts in an anhydrous condition at 108° (Ber. **15**, 410). The production of *acetochloroamylamide,* $CH_3CO\cdot NClC_5N_{11}$, from hypochlorous acid and acetoamylamide, and from acetic anhydride and chloroamylamine in glacial acetic acid (Ber. **34**, 1613), is taken as a demonstration that in such compounds the halogen atom is joined to the nitrogen atom.

Higher homologous primary Acid Amides :

Propionamide, m.p. 75°, b.p. 210°.

n-*Butyramide,* m.p. 115°, b.p. 216°. iso*Butyramide,* m.p. 128°, b.p. 216–220°.

n-*Valeramide,* m.p. 114–116°. *Trimethylacetamide,* m.p. 153–154°, b.p. 212°.

n-*Capronamide,* m.p. 100°, b.p. 225° ; *Methyl*-n-*propylacetamide,* m.p. 95° ; *Methyl*iso*propylacetamide,* m.p. 129° ; iso*Butylacetamide,* m.p. 120° ; *Diethylacetamide,* m.p. 105°, b.p. 230–235° ; *Œnanthamide,* m.p. 95°, b.p. 250–258° ; n-*Caprylamide,* m.p. 105–106° ; *Pelargonamide,* m.p. 92–93° ; n-*Caprinamide,* m.p. 98°.

Lauramide, m.p. 102°, b.p. 199–200°/12·5 mm. ; *Tridecylamide,* m.p. 98·5° ; *Myristamide,* m.p. 102°, b.p. 217°/12 mm. ; *Palmitamide,* m.p. 106°, b.p. 235–236°/12 mm. ; *Stearamide,* m.p. 108·5–109°, b.p. 250–251°/12 mm. (Ber. **15**, 977, 1729 : **19**, 1433 : **24**, 2781 : **26**, 2840).

7. ACID HYDRAZIDES

The mono-acyl hydrazides (C. 1002, I. 21) are obtained together with the *sym.*-diacylhydrazines by the interaction of hydrazine and the esters, while the latter are also prepared from hydrazine and the acid anhydrides (Ber. **34**, 187). The latter-named bodies can also be obtained by heating monoacyl hydrazines, and by treating them with iodine. *sym.*-Diacetohydrazide, heated with acetic anhydride, yields triacetohydrazide and tetraacetohydrazide (Ber. **32**, 796).

The mono-acyl hydrazides condense with aldehydes and ketones with the elimination of water. The *sym.*-diacylhydrazines react with zinc chloride or phosphorus pentoxide to form dialkylfurodiazoles ; with alcoholic ammonia, yielding dialkylpyrrodiazoles ; and with phosphorus pentasulphide, forming dialkylthiodiazoles (Ber. **32**, 797).

Acetohydrazide, $CH_3CONH\cdot NH_2$, m.p. 62°. *Acetobenzalhydrazine,* $CH_3CO\cdot NH\cdot N:CH\cdot C_6H_5$, m.p. 134°. sym.-*Diacetohydrazine,* m.p. 138° ; b.p. 209°/15 mm. ; *triacetohydrazine,* b.p. 181°/15 mm. ; *tetraacetohydrazine,* m.p. 85°, b.p. 141°/15 mm.

8. ACID AZIDES

The azides, $R\cdot CO\cdot N_3$, show some similarities in behaviour to the acid halides, but will be treated here on account of their relation to the hydrazides.

They are formed by the action of sodium nitrite on the hydrochlorides of the monoacyl hydrazines.

When heated in indifferent solvents, the azides break down into nitrogen and *iso*cyanic esters. (Curtius transformation, see p. 191 and Ber. **42**, 3356.) If hydroxylic solvents are employed, the products are those derived from the *iso*cyanate and the solvent, *e.g.* in aqueous solution, dialkylureas and in alcoholic urethanes :

$$CH_3\cdot CO\cdot N_3 \longrightarrow [CH_3\cdot CO\cdot N<] + N_2 \longrightarrow CH_3\cdot N:C:O$$

Propionazide, $C_2H_5\cdot CO\cdot N_3$, is a colourless, mobile, volatile liquid with a pungent smell (J. pr. Chem. [2] **64**, 408).

9. NITRILES OR ALKYL CYANIDES

The nitriles or alkyl cyanides are the alkyl esters, $R\cdot CN$, of hydrocyanic acid. Being intermediate steps in the synthesis of the fatty acids from the alcohols, these nitriles merit especial consideration.

General methods of preparation :

(1) Nucleus-synthesis from the alcohols : (*a*) by heating the alkyl halides with potassium cyanide in alcoholic solution to 100° ; (*b*) by the distillation of potassium alkyl sulphates with potassium cyanide (hence the name alkyl cyanides) :

(1*a*) $C_2H_5I + KNC = C_2H_5CN + KI$
(1*b*) $KSO_4{\cdot}C_2H_5 + KNC = C_2H_5CN + K_2SO_4.$

*iso*Cyanides (p. 293) form to a slight extent in the first reaction. They can be removed by shaking the distillate with aqueous hydrochloric acid (whereby the *iso*nitrile is converted into formic acid and a primary amine), until the unpleasant odour of the *iso*cyanides has disappeared, then neutralizing with sodium carbonate and drying the nitriles with calcium chloride.

(2) By the action of the magnesium alkyl halides on cyanogen or cyanogen chloride (Compt. rend. **152,** 388 : *cf. ibid.* **155,** 44).

(3) By heating alkyl *iso*cyanides or alkyl carbylamines (p. 293) :

$$CH_3CH_2NC \xrightarrow{250^\circ} CH_3CH_2CN.$$

(4) By the dry distillation of ammonium salts of the acids with P_2O_5, or some other dehydrating agent (hence the term acid nitrile).

$$\underset{\text{Ammonium acetate.}}{CH_3{\cdot}CO{\cdot}O{\cdot}NH_4} - 2H_2O = \underset{\text{Acetonitrile.}}{CH_3{\cdot}CN.}$$

The corresponding acid amide is an intermediate product.

(5) By the removal of water from the amides of the acids when these are heated with P_2O_5, P_2S_5, or phosphorus pentachloride (see amide chlorides, p. 327) :

$$CH_3{\cdot}CO{\cdot}NH_2 + PCl_5 = CH_3{\cdot}CN + POCl_3 + 2HCl$$
$$5CH_3{\cdot}CO{\cdot}NH_2 + P_2S_5 = 5CH_3{\cdot}CN + P_2O_5 + 5H_2S.$$

(6) By the distillation of fatty acids with potassium thiocyanate (Ber. **5,** 669), or lead thiocyanate (Ber. **25,** 419), during which a complicated reaction occurs. It is assumed that a thioamide is first formed which loses H_2S, changing into the nitrile, or that a carboxyl is exchanged for a CN-group.

(7) Primary amines, containing more than five carbon atoms, are converted, by potassium hydroxide and bromine, into nitriles :

$$C_7H_{15}CH_2NH_2 + 2Br_2 + 2KOH = C_7H_{15}CH_2NBr_2 + 2KBr + 2H_2O$$
$$C_7H_{15}CH_2NBr_2 + 2KOH = C_7H_{15}CN + 2KBr + 2H_2O.$$

As the primary amines can be obtained from acid amides containing a carbon atom more, these reactions will serve for the breaking-down of the fatty acids (p. 308).

(8) Nitriles result when aldoximes are heated with acetic anhydride or with thionyl chloride (Ber. **28,** R. 227) :

$$CH_3CH : N{\cdot}OH + (CH_3CO)_2O = CH_3C \vdots N + 2CH_3{\cdot}COOH.$$

(9) By the catalytic decomposition of the aldehyde phenylhydrazones in the presence of cuprous chloride (Ber. **43,** 2296) :

$$C_4H_9CH : N{\cdot}NHC_6H_5 \longrightarrow C_4H_9CN + C_6H_5NH_2.$$

This method only gives good yields in the case of the higher aldehyde derivatives : the principal yield from the lower phenylhydrazones consists of indole derivatives.

(10) On the application of heat to cyanoacetic acid and alkylcyanoacetic acids, nitriles result:

$$CNCH_2 \cdot CO_2H = CNCH_3 + CO_2.$$

The nitriles occur already formed in bone-oils and in gas tar.

Historical.—*Pelouze* (1834) discovered propionitrile on distilling barium ethyl sulphate with potassium cyanide (Ann. **10**, 249). *Dumas* (1847) obtained acetonitrile by distilling ammonium acetate alone, or with P_2O_5; the same occurred with the latter reagent and acetamide (p. 323). *Dumas*, *Malaguti* and *Leblanc* (Ann. **64**, 334) on the one hand, and *Frankland* and *Kolbe* (Ann. **65**, 269, 288, 299) on the other, demonstrated (1847) the conversion of the nitriles into their corresponding acids by means of potassium hydroxide or dilute acids, and thus showed what importance the acid nitriles possessed for synthetic organic chemistry.

Properties and Reactions.—The nitriles are liquids, usually insoluble in water, possessing an ethereal odour, and distilling without decomposition.

Their reactions are based upon the easy disturbance of the triple union between nitrogen and carbon, and are mostly additive reactions. Acid nitriles may be considered to be unsaturated compounds, in the same sense as are the aldehydes and ketones (pp. 27, 255). Their neutral character distinguishes them from hydrocyanic acid, the nitrile of formic acid, which they resemble as regards the reactions of their $C \equiv N$-group.

(1) They are reduced by nascent hydrogen to the primary amines (*Mendius*). This reduction is most readily carried out by sodium and alcohol (Ber. **22**, 812: C. 1908, II. 676). By catalytic hydrogenation, some secondary and tertiary amine is also formed (Ber. **42**, 1553: **56**, 1988).

(2) The nitriles unite with the halogen acids, forming amide and imide halides (p. 327).

(3) Under the influence of concentrated sulphuric acid they take up water and become converted into acid amides. When heated to 100° with water the acid amides first formed absorb a second molecule of water and change to the fatty acid and ammonia. The nitriles are more readily hydrolysed by heating them with alkalis or dilute acids (hydrochloric or sulphuric acid). Esters are produced when the acids, in a solution of absolute alcohol, act on the nitriles.

(4) The nitriles form thiamides with H_2S (p. 328).

(5) They combine with alcohols and HCl to form imido-ethers (p. 328).

(6) With fatty acids and fatty acid anhydrides they yield secondary and tertiary amides (p. 322).

(7) The nitriles become converted into amidines with ammonia and the amines (p. 328).

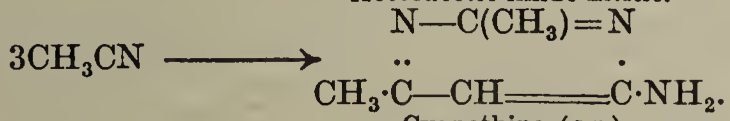
(8) Hydroxylamine unites with them to form amidoximes (p. 329).

(9) Metallic sodium induces in them peculiar polymerizations. In ethereal solution, dimolecular nitriles result: imides of β-ketonic nitriles. All these reactions depend upon the additive power of the nitriles, the triple carbon-nitrogen union being broken. If, however, sodium acts on the pure nitriles at a temperature of 150° the pro-

ducts are trimolecular nitriles, so-called cyanalkines, which are pyrimidine derivatives :

$$2CH_3CN \longrightarrow CH_3{\cdot}C(NH){\cdot}CH_2{\cdot}CN$$

Acetoacetic imide nitrile.



Cyanethine (*q.v.*).

Acetonitrile, *Methyl cyanide* [Ethane nitrile], CH_3CN, m.p. − 41°, b.p. 81·6°, $D_{15} = 0{\cdot}789$, is a liquid with an agreeable odour. It is usually prepared by distilling acetamide with P_2O_5. Consult the general description of acid nitriles for its methods of formation, its history and its reactions. It may, however, be mentioned here that acetonitrile can be produced from hydrocyanic acid and diazomethane (Ber. **28**, 857). Acetonitrile is a good solvent for many organic compounds and forms crystalline compounds with many salts, *e.g.* $CuCl_2{\cdot}2CH_3CN$ (Ber. **47**, 247).

Higher Homologous Nitriles.—*Propionitrile, Ethyl cyanide,* [Propane nitrile], $C_2H_5{\cdot}CN$, b.p. 98°, D_0 0·801.

n-*Butyronitrile,* b.p. 118·5°, has the odour of bitter-almond oil. iso*Butyronitrile,* b.p. 107°.

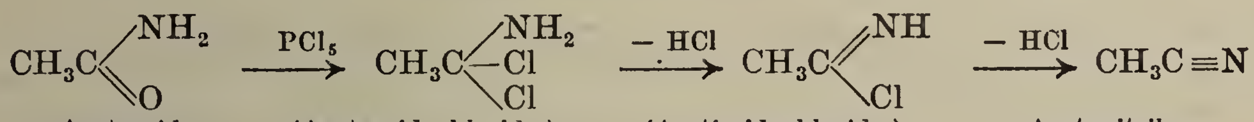
n-*Valeronitrile,* b.p. 140·4° ; iso*Valeronitrile,* b.p. 129° ; *Methylethylacetonitrile,* b.p. 125° ; *Trimethylacetonitrile,* m.p. 15–16°, b.p. 105–106°.

iso*Butylacetonitrile,* b.p. 154° ; *Diethylacetonitrile,* b.p. 144–146° ; *Dimethylethylacetonitrile,* b.p. 128–130° ; n-*Œnanthonitrile,* b.p. 175–178° ; n-*Caprylonitrile,* b.p. 198–200° ; *Pelargonitrile,* b.p. 214–216° ; *Methyl*-n-*hexylacetonitrile,* b.p. 206° ; *Lauronitrile,* b.p. 198°/100 mm. ; *Tridecylonitrile,* b.p. 275° ; *Myristonitrile,* m.p. 19°, b.p. 226·5°/100 mm. ; *Palmitonitrile,* m.p. 29°, b.p. 251·5°/100 mm. ; *Cetyl cyanide,* m.p. 53° ; *Stearonitrile,* m.p. 41°, b.p. 274·5°/100 mm.

Several classes of compounds bear genetic relations to the acid amides and nitriles, these will be considered after the nitriles.

10. AMIDOCHLORIDES and 11. IMIDOCHLORIDES (*Wallach,* Ann. 184, 1)

The amidochlorides are the first unstable products formed during the action of PCl_5 on acid amides. They lose hydrochloric acid and become converted into imidochlorides, which by a further separation of hydrochloric acid yield nitriles :



Acetamide. (Acetamidochloride.) (Acetimidochloride.) Acetonitrile.

The addition of HCl to the nitriles produces the imidochlorides. Hydrobromic and hydriodic acids are added more readily than hydrochloric acid to nitriles (Ber. **25**, 2541).

The imidochlorides derived from amides of the types $CH_2R{\cdot}CONHR'$ and $CHR_2{\cdot}CONHR'$ are represented by von Braun and his collaborators by the formulæ $R{\cdot}CH{=}CCl{\cdot}NHR'$ and $R_2C : CCl{\cdot}NHR'$; this formula accounts for the formation of amidines such as $CH_3C(: NPh){\cdot}NPh{\cdot}CCl : CH_2$, formed from acetphenylimidochloride by loss of HCl and for the formation of α-bromo acids from the readily-formed addition product of the imidochloride and bromine (Ber. **60**, 92 : Ann. **453**, 113).

If a hydrogen atom of the amide group be replaced by an alcohol radical, the imidochlorides are more stable. On being heated, however, they lose hydrochloric acid in part and pass into chlorinated bases.

(1) Water changes the imidochlorides back into acid amides. The chlorine atom of these bodies is as reactive as the chlorine atom of the acid chlorides. (2) Ammonia and the primary and secondary amines change the imidochlorides to amidines (p. 328). (3) Hydrogen sulphide converts the imidochlorides into thiamides.

12. IMIDO-ETHERS* (*Pinner*, Ber. **16**, 353, 1654: **17**, 184, 2002)

The imido-ethers may be regarded as the esters of the imido-acids, $R'\cdot C \lessgtr\begin{smallmatrix}NH\\OH\end{smallmatrix}$, a tautomeric formula of the acid amides, according to which the latter behave in many reactions (comp. also the Thiamides).

The hydrochlorides of the imido-ethers are produced by the action of HCl on a cooled ethereal solution of a nitrile with an alcohol (in molecular quantities):

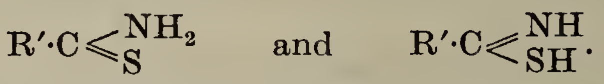
$$CH_3CN + C_2H_5OH + HCl = CH_3C \lessgtr\begin{matrix}NH\cdot HCl.\\OC_2H_5\end{matrix}$$

Acetimido-ether.

Formimido-ether, (p. 288). *Acetimido-ethyl ether*, b.p. 94°, when liberated from its HCl-salt by means of NaOH, is a peculiar-smelling liquid. Ammonia and the amines convert the imido-ethers into amidines. Shaking the imido-ether hydrochlorides with alcohol produces ortho-esters (p. 330).

13. THIAMIDES

As in the case of the acid amides (p. 321), so here with the thiamides two tautomeric formulas are possible:



$$R'\cdot C \lessgtr\begin{matrix}NH_2\\S\end{matrix} \quad \text{and} \quad R'\cdot C \lessgtr\begin{matrix}NH\\SH\end{matrix}.$$

The thiamides are formed (1) by the action of phosphorus sulphide on the acid amides; (2) by the addition of H_2S to the nitriles (p. 326):

$$\underset{\text{Acetonitrile.}}{CH_3\cdot CN} + H_2S = \underset{\text{Thiacetamide.}}{CH_3\cdot CS\cdot NH_2}.$$

Reactions.—(1) The thiamides are readily broken up into fatty acids, H_2S NH_3 and amines.

(2) They yield thiazole derivatives with chloroacetic ester, chloroacetone, and similar bodies.

(3) Ammonia converts them into amidines.

(4) The action of hydroxylamine results in the production of amidoximes.

(5) Reduction produces primary and secondary amines (Ann. **431**, 191).

Thioformamide, $H\cdot CSNH_2$, m.p. (anhydrous) 28–29°, is obtained from P_2S_5 and formamide (Ber. **42**, 1911).

Thioacetamide, m.p. 108° (Ann. **192**, 46; Ber. **11**, 340). *Thiopropionamide*, m.p. 42–43° (Ann. **259**, 229).

14. THIO-IMIDO-ETHERS

are derived from the imidothiohydrin form of the thioamides. They are prepared, analogously to the imido-ethers, from the nitriles with mercaptans and HCl (Ber. **36**, 3464). *Acetimido-thiophenyl ether*, $CH_3C \lessgtr\begin{smallmatrix}NH\\SC_6H_5\end{smallmatrix}$, is obtained from its hydrochloride by the action of sodium hydroxide. It is an unstable yellow syrup. The *hydrochloride*, m.p. 120° (decomp.), is prepared from acetonitrile, thiophenol (Vol. II) and HCl.

15. AMIDINES, $R\cdot C \lessgtr\begin{smallmatrix}NH\\NH_2\end{smallmatrix}$ (Ann. **184**, 121: **192**, 46)

The amidines, containing an amide and imide group, whose hydrogen atoms are replaceable by alkyls, may be considered to be derivatives of the acid amides, in which the carbonyl oxygen is replaced by the imide group:

$$\underset{\text{Acetamide.}}{CH_3CONH_2} \qquad \underset{\text{Acetamidine.}}{CH_3C(NH)NH_2}.$$

They are produced:

(1) From the imide chlorides and thiamides, by the action of ammonia or amines.

(2) From the nitriles by heating them with ammonium chloride.

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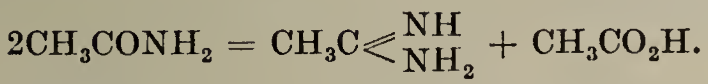
* *A. Pinner*, Die Imidoaether und ihre Derivate, 1892.

(3) From the amides of the acids when treated with HCl (Ber. **15**, 208):

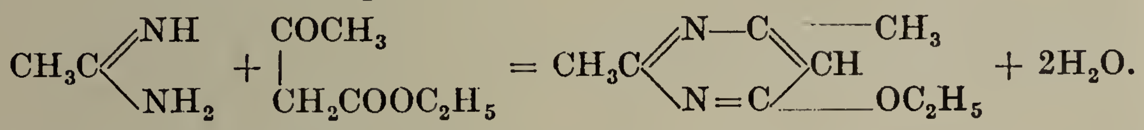


$$2CH_3CONH_2 = CH_3C{<}^{NH}_{NH_2} + CH_3CO_2H.$$

(4) From the imido-ethers (p. 328) when acted on with ammonia and amines (Ber. **16**, 1647: **17**, 179).

The amidines are mono-acid bases. In a free condition they are very unstable. The action of various reagents on them induces absorption of water, the imide group splits off, and acids or amides of the acids are regenerated.

β-Ketonic esters convert them into pyrimidines, *e.g.* acetamidine hydrochloride and acetoacetic ester yield ethoxydimethylpyrimidine, m.p. 192° (comp. polymerization of acetonitrile, p. 327):



Formamidine (p. 289).

Acetamidine, Acediamine, Ethenyl amidine, $CH_3C(NH_2)NH$; *hydrochloride*, m.p. 163°. The acetamidine, separated by alkalis, reacts strongly alkaline and readily breaks up into NH_3 and acetic acid.

16. HYDROXAMIC ACIDS, $R{\cdot}C{<}^{N{\cdot}OH}_{OH}$

These are produced by the action of hydroxylamine on acid amides, esters, and chlorides. They are characterized by containing an oximido- or *iso*nitroso-group in place of a carboxylic oxygen atom (Ber. **22**, 2854). Another method of preparation is from aldehydes and nitrohydroxylaminic acid salts, O:N(OH):N(OH) (C. 1901, II. 770). (Reaction of Angeli-Rimini: see p. 230.)

$$CH_3COH + N_2O_3H_2 = CH_3C(NOH)OH + HNO_2.$$

Benzene sulphohydroxamic acid, $C_6H_5SO_2NHOH$, behaves similarly, by forming acyl hydroxamic acids and benzene sulphinic acid, $C_6H_5SO_2H$, with aldehydes (C. 1901, II. 99).

They are crystalline compounds, acid in character (Gazzetta, **40**, I. 102), and form an insoluble copper salt in ammoniacal copper solutions. Ferric chloride imparts a cherry-red colour to both their acid and neutral solutions.

Acetohydroxamic acid, $CH_3C(NOH)OH + \frac{1}{2}H_2O$, m.p. 59°. It dissolves very easily in water and alcohol, but not in ether.

In addition to the general methods of preparation it is also obtained by heating hydroxylamine acetate to 90°.

Formhydroxamic acid (see p. 289).

17. HYDROXIMIC ACID CHLORIDES, $RC{<}^{NOH}_{Cl}$

When chlorine is passed into a solution of acetaldoxime, a precipitate of colourless crystals of *nitrosochloroethane*, $CH_3{\cdot}CHCl{\cdot}NO$, m.p. 65°, is formed. This melts to form a blue liquid and dissolves in ether forming a blue solution. From both the colour gradually disappears on standing owing to a change into *acetohydroximic acid chloride*, $CH_3{\cdot}CCl(:NOH)$, m.p. − 3°, a colourless, easily decomposed liquid. Silver nitrite converts it into acetonitrolic acid (see p. 184); chlorine produces *nitrosodichloroethane*, $CH_3CCl_2{\cdot}NO$, b.p. 68°, a deep-blue oil (Ber. **35**, 3101). Acetohydroximic acid chloride is also obtained directly by the action of chlorine on a hydrochloric acid solution of acetaldoxime (Ber. **40**, 1677).

18. NITROLIC ACIDS, $R{\cdot}C{<}^{N{\cdot}OH}_{NO_2}$ (p. 184)

As these bodies are genetically related to the mononitroparaffins, they have already been discussed immediately after them.

19. AMIDOXIMES or OXAMIDINES, $R{\cdot}C{<}^{N{\cdot}OH}_{NH_2}$

These compounds may be regarded as amidines, in which a H atom of the amide or imide group has been replaced by hydroxyl. They are formed: by the action of hydroxylamine on the amidines (p. 328); by the addition of hydroxylamine to the nitriles (Ber. **17**, 2746):

$$\underset{\text{Acetonitrile.}}{CH_3CN} + NH_2OH = \underset{\text{Acetamidoxime.}}{CH_3C{<}\begin{smallmatrix}NH_2\\NOH\end{smallmatrix}},$$

and by the action of hydroxylamine on thiamides (Ber. **19**, 1668):

$$CH_3CSNH_2 + NH_2OH = CH_3{\cdot}C{<}\begin{smallmatrix}NH_2\\NOH\end{smallmatrix} + H_2S.$$

The amidoximes are crystalline, very unstable compounds, which readily break down into hydroxylamine, and the acid amides or acids.

Formamidoxime (p. 289).

Ethenyl amidoxime, $CH_3C{<}\begin{smallmatrix}NOH\\NH_2\end{smallmatrix}$, m.p. 135°. *Hexenyl amidoxime*, m.p. 48°. *Heptenyl amidoxime*, m.p. 48–49° (Ber. **25**, R. 637). *Lauryl amidoxime*, m.p. 92–92·5°. *Myristyl amidoxime*, m.p. 97°. *Palmityl amidoxime*, m.p. 101·5–102°. *Stearyl amidoxime*, m.p. 106–106·5° (Ber. **26**, 2844).

20, 21. HYDROXAMIC OXIMES AND NITROSOXIMES. (NITROSOLIC ACIDS)

These and allied bodies are obtained from the hydroximic acid chlorides and nitrolic acids (Ann. **353**, 65: Ber. **40**, 1676).

Acetohydroxamic oxime, $CH_3C{<}\begin{smallmatrix}NHOH\\NOH\end{smallmatrix}$, results from the interaction of acetohydroximic acid chloride and hydroxylamine, or from the reduction of ethylnitrolic acid (p. 184) with sodium amalgam. It is unstable in the free state, but is known as a colourless *hydrochloride*, m.p. 156° (decomp.), and as a red-brown *copper salt*, $C_2H_4O_2N_2Cu + 2H_2O$. Dilute alkali changes it into an unstable strongly coloured *azo*-body, $CH_3C(:NOH){\cdot}N{=}N{\cdot}C(:NOH)CH_3$, which partially changes into its more stable and equally coloured isomer, *ethylazaurolic acid*, $CH_3C(:NOH){\cdot}NH{\cdot}N:C(NO)CH_3$, and partially breaks down into ethylnitrosolic acid and acetamide oxime:

$$CH_3C(NOH){\cdot}N{=}N{\cdot}C(:NOH)CH_3 \xrightarrow{H_2O} CH_3C(:NOH)NO + H_2NC(NOH)CH_3.$$

Acetonitroso-oxime, Ethylnitrosolic acid, $CH_3C{<}\begin{smallmatrix}NO\\NOH\end{smallmatrix}$, is prepared from acetohydroxamic oxime by oxidation with bromine. It is characterized by its deep-blue potassium salt, $C_2H_3N_2O_2K$. It is readily decomposed by acids.

For further reactions, see above.

22, 23. HYDRAZIDINE AND HYDRAZO-OXIMES

such as $RC{<}\begin{smallmatrix}N{\cdot}NHC_6H_5\\NH_2\end{smallmatrix}$ and $RC{<}\begin{smallmatrix}NH{\cdot}NHC_6H_5\\NOH\end{smallmatrix}$ see Vol. II, and Ber. **35**, 3271.

24. ORTHO-FATTY ACID DERIVATIVES

The ortho-esters of the fatty acids are obtained similarly to orthoformic ester (p. 290) (1) from the imido-ether hydrochlorides (p. 328) and alcohols (Ber. **40**, 3020); (2) from the orthotrichlorides and sodium alcoholate; (3) synthetically from the orthocarbonic acid esters and alkyl magnesium halides (Ber. **38**, 561).

Orthoacetic triethyl ester, $CH_3C(OC_2H_5)_3$, b.p. 145°/748 mm., 42°/13 mm., is a colourless pleasant-smelling liquid, but differing in odour from the ordinary ester.

Orthopropionic ester, $CH_3CH_2C(OC_2H_5)_3$, b.p. 161°/66 mm., 54°/12 mm.

Orthoacetyl trichloride, methylchloroform, ethenyl trichloride. ααα-Trichloroethane, CH_3CCl_3, b.p. 74·5°, is formed together with ααβ-trichloroethane, by the action of chlorine on ethylidine chloride (Ann. **195**, 183).

Orthoacetic tripiperide, $CH_3{\cdot}C(NC_5H_{10})_3$, b.p. 261°, is obtained by heating together methylchloroform and piperidine. It forms a strongly alkaline, colourless liquid, of a peculiar odour: *hydrochloride*, $CH_3{\cdot}C(N{\cdot}C_5H_{10}{\cdot}HCl)_3$, does not melt at 260°.

HALOGEN SUBSTITUTION PRODUCTS OF THE FATTY ACIDS

The halogen substitution products of the fatty acids are, in general, produced by the same methods as those employed for the preparation of the halogen derivatives of the paraffins.

(1) *Direct Substitution of the Fatty Acids.*

(*a*) The chloro acids are obtained by the action of chlorine on the fatty acids in sunlight, or in the presence of catalysts such as iodine, sulphur (Ber. **25**, R. 797) or phosphorus (Ber. **24**, 2209), or by the action of sulphuryl chloride on the fatty acids (C. 1905, I. 414).

(*b*) The bromo acids are also obtained by direct bromination of the fatty acids (Mechanism of reaction, see J.C.S. **123**, 2233), or by heating them with water and bromine in a sealed tube, or by the use of sulphur (Ber. **25**, 3311) or phosphorus as catalysts.

(*c*) The iodo acids are obtained by iodination by iodine and iodic acid (to reduce the hydriodic acid produced), or from the bromo acids and potassium iodide.

The *acid chlorides*, *bromides*, or *anhydrides* are more readily substituted than the free acids. This reaction can be brought about most suitably by the addition of the required quantity of chlorine dissolved in CCl_4 to a solution of the chloride in the same solvent. Each liquid is cooled externally, and the mixture is made in full sunlight (Ber. **34**, 4047). When chlorine or bromine, in the presence of phosphorus, acts on the fatty acids (method of Hell-Volhard), acid chlorides and bromides result; these are then subjected to substitution. The final products are halogen-acid chlorides or halogen-acid bromides:

$$3CH_3{\cdot}CO_2H + P + 11Br = 3CH_2Br{\cdot}COBr + HPO_3 + 5HBr.$$

However, substitution only takes place in a mono-alkyl or dialkyl-acetic acid at the α-carbon atom. Hence, trimethylacetic acid cannot be chlorinated or brominated. Consequently the behaviour of a fatty acid towards chlorine or bromine and phosphorus indicates whether or not a trialkyl-acetic acid is present (Ber. **24**, 2209).

Mechanism of Hell-Volhard reaction, see Ber. **45**, 1913: **46**, 2162.

(2) *Addition of Halogen Acids to Unsaturated Monocarboxylic Acids.*—The halogen enters at a point as far as possible from the carboxyl group, *e.g.*:

$$\underset{\text{Acrylic acid.}}{CH_2:CH{\cdot}CO_2H}\left\{\begin{array}{lll} \xrightarrow{HCl} & CH_2Cl{\cdot}CH_2{\cdot}CO_2H & \beta\text{-Chloro-} \\ \xrightarrow{HBr} & CH_2Br{\cdot}CH_2{\cdot}CO_2H & \beta\text{-Bromo-} \\ \xrightarrow{HI} & CH_2I{\cdot}CH_2{\cdot}CO_2H & \beta\text{-Iodo-} \end{array}\right\}\text{propionic acid.}$$

(3) *Addition of Halogens to Unsaturated Monocarboxylic Acids.*—Whenever possible the chlorine is allowed to act in a CCl_4 solution. Bromine often reacts without the help of a solvent, also in the presence of water, CS_2, glacial acetic acid and chloroform.

(4) Action of the *halogen acids* (*a*) *on hydroxymonocarboxylic acids*:

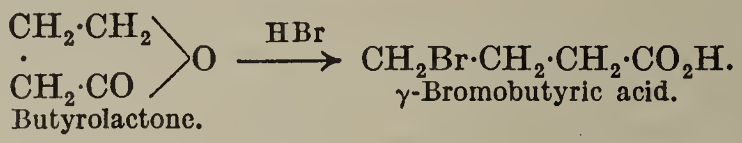
$$\underset{\text{Hydracrylic acid.}}{CH_2(OH)CH_2CO_2H} \xrightarrow[120^\circ]{HCl} \underset{\substack{\beta\text{-Chloropropionic}\\ \text{acid.}}}{CH_2Cl{\cdot}CH_2{\cdot}CO_2H}$$

$$\underset{\text{Lactic acid.}}{CH_3CH(OH)CO_2H} \xrightarrow{HBr} \underset{\substack{\alpha\text{-Bromopropionic}\\ \text{acid.}}}{CH_3CHBrCO_2H}$$

$$\underset{\text{Glyceric acid.}}{CH_2(OH)CH(OH)CO_2H} \xrightarrow{HI} \underset{\substack{\beta\text{-Iodopropionic}\\ \text{acid.}}}{CH_2I{\cdot}CH_2{\cdot}CO_2H}$$

In the case of hydriodic acid, reduction of a polyhydroxy acid may occur, with formation of a *mono*halogen derivative.

(4*b*) *On lactones,* cyclic anhydrides of γ- or δ-hydroxy acids :



$$\left.\begin{matrix} CH_2{\cdot}CH_2 \\ CH_2{\cdot}CO \end{matrix}\right\rangle O \xrightarrow{HBr} CH_2Br{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H.$$

Butyrolactone. γ-Bromobutyric acid.

(5) Action of the phosphorus halides, particularly PCl_5 or thionyl chloride, on hydroxymonocarboxylic acids or their nitriles or esters (C. 1898, I. 22 : Compt. rend. **152,** 1601). The product is the chloride of a chlorinated acid, which water transforms into the acid :

$$CH_3{\cdot}CHOH{\cdot}COOH + 2PCl_5 = CH_3{\cdot}CHCl{\cdot}COCl + 2POCl_3 + 2HCl.$$

Lactic acid. α-Chloropropionyl chloride.

Furthermore, halogen fatty acids are obtained like the parent acids (6) by the *oxidation of chlorinated alcohols or aldehydes* (p. 238) with nitric acid, chromic acid, potassium permanganate or potassium chlorate (Ber. **18,** 3336) :

$$CH_2Cl{\cdot}CHCl{\cdot}CH_2OH \xrightarrow{2O} CH_2Cl{\cdot}CHCl{\cdot}CO_2H$$

αβ-Dichlorhydrin. αβ-Dichloropropionic acid.

$$CCl_3CHO \xrightarrow{O} CCl_3COOH$$

Chloral. Trichloroacetic acid.

(7) The formation of halogen derivatives of acetyl chloride and bromide by the autoxidation of halogen derivatives of ethylene deserves mention (see p. 124) :

$$CH_2{=}CBr_2 \longrightarrow CH_2Br{\cdot}COBr. \quad CHCl{=}CCl_2 \longrightarrow CHCl_2{\cdot}COCl.$$

(8) By the action of halogen acids on diazo-fatty acid esters (see Glyoxylic acid) :

$$CHN_2{\cdot}CO_2C_2H_5 + HCl = CH_2Cl{\cdot}CO_2C_2H_5 + N_2.$$

(9) When the halogens act on diazo-fatty acid esters :

$$CHN_2CO_2C_2H_5 + I_2 = CHI_2CO_2C_2H_5 + N_2.$$

Isomerism and Nomenclature.—Structurally isomeric halogen substitution products of the fatty acids are first possible with propionic acid. To indicate the position of the halogen atoms, the carbon atom to which the carboxyl group is attached is marked α, whilst the other carbon atoms are successively called β, γ, δ, ε, etc. The two monochloropropionic acids are distinguished as α- and β-chloropropionic acids, whilst the three isomeric dichloropropionic acids are the αα-, ββ- and αβ-dichloropropionic acids, etc. In the " Geneva Nomenclature " the C-atom of the COOH group is numbered 1, so that $CH_3{\cdot}CHCl{\cdot}CO_2H$, for example, is 2-chloropropionic acid, *not* 1-chloropropionic acid.

Properties and Reactions.—The introduction of substituting halogen atoms increases the acid character of the fatty acids. The halogen fatty acids, like the parent acids, yield, by analogous treatment, esters, chlorides, anhydrides, amides, nitriles, etc.

On the velocity of ester formation and the electric conductivity of the α-, β-, γ-, and δ-halogen fatty acids, see Ann. **319, 369**: Gazzetta. **40,** I. 294.

(1) Nascent hydrogen causes the halogen substitution products of the fatty acids to revert to the parent acids—*retrogressive substitution.*

In general, the monohalogen fatty acids resemble in their reactions the alkyl halides.

(2) Boiling water, alkali hydroxides, or an alkali carbonate solution generally brings about an exchange of hydroxyl for the halogen atom (Ann. **342,** 115).

In monohalogen products, the position of the halogen atom, with reference to carboxyl, materially affects the course of the reaction: α-halogen acids yield α-hydroxy acids, β-halogen acids split off the halogen acid and become converted into unsaturated acids with the formation also of β-hydroxy acids (Ann. **342,** 127); γ-halogen acids, on the contrary, yield γ-hydroxy acids, which readily yield lactones (Ann. **219,** 322):

$$CH_2ClCOOH \xrightarrow{H_2O} CH_2(OH)CO_2H$$

$$CH_2ClCH_2COOH \xrightarrow{H_2O} CH_2{=}CHCO_2H$$

$$CH_2ClCH_2CH_2COOH \xrightarrow{H_2O} CH_2\overline{OCH_2CH_2C}O.$$

The β-halogen fatty acids are converted into β-lactones $R\cdot CH(\overline{O)\cdot CH_2C}O$ when the aqueous solution of their sodium salts is agitated with chloroform at 40° (C. 1916, II. 557).

(3) Ammonia converts the halogen acids into the corresponding amino acid.

(4) The amides of α-bromo-fatty acids lose HBr and HCN when heated with potassium hydroxide, an aldehyde or ketone containing one carbon atom less being formed (Monatsh. **29,** 69):

$$(CH_3)_2CBr\cdot CONH_2 \longrightarrow (CH_3)_2CO + HCN + HBr.$$

Nucleus-synthetic Reactions.—(5) Potassium cyanide produces cyano-fatty acids—the mononitrile of dibasic acids, which hydrochloric acid changes to dibasic acids. They will be considered after the latter:

$$\underset{\text{Chloroacetic acid.}}{CH_2ClCO_2H} \xrightarrow{KCN} \underset{\text{Cyanoacetic acid.}}{CH_2{<}\begin{smallmatrix}CO_2H\\ CN\end{smallmatrix}} \xrightarrow{2H_2O,HCl} \underset{\text{Malonic acid.}}{CH_2{<}\begin{smallmatrix}CO_2H\\ CO_2H.\end{smallmatrix}}$$

(6) Dicarboxylic acids have also been obtained from monohalogen carboxylic acids by means of metals:

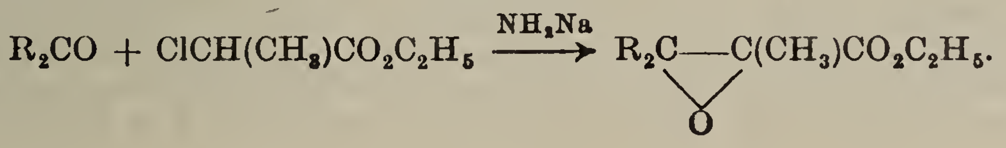
$$2CH_2ICH_2CO_2H + 2Ag = \underset{\text{Adipic acid.}}{\begin{array}{c}CH_2\cdot CH_2\cdot CO_2H\\ \cdot\\ CH_2\cdot CH_2\cdot CO_2H\end{array}} + 2AgI.$$

(7) The esters of the monohalogen fatty acids have been applied in connection with the acetoacetic ester and malonic ester syntheses, and as results we have β-ketone dicarboxylic acids, β-ketone-tricarboxylic acids, and tri- and tetracarboxylic acids.

(8) The esters of the halogen fatty acids form with zinc or magnesium organo-metallic compounds; in the presence of aldehydes and ketones, salts of the higher hydroxy-fatty acid esters are formed:

$$RCHO + BrCH(CH_3)CO_2C_2H_5 \xrightarrow{Zn} RCH(OZnBr)\cdot CH(CH_3)CO_2C_2H_5.$$

(9) The final product of condensation of α-halogen fatty acid esters and ketones by means of sodium amide are the ethylene oxide carboxylic esters (glycidic acid esters):



$$R_2CO + ClCH(CH_3)CO_2C_2H_5 \xrightarrow{NH_2Na} R_2C\text{—}C(CH_3)CO_2C_2H_5.$$

Chloroformic acid, $Cl\cdot COOH$, is regarded as the chloride of carbonic acid. It will be discussed after carbonic acid.

Substitution Products of Acetic Acid

Monochloroacetic acid, $CH_2Cl\cdot CO_2H$, m.p. 62°, b.p. 185–187°, solidifies after fusion to an *unstable modification*, m.p. 52°. This slowly reverts spontaneously to the ordinary acid (Ber. **26**, R. 381). On the preparation of the acids from acetic acid and sulphuryl chloride, see C. 1905, I. 414.

Preparation by chlorination of acetic acid in presence of iodine, red phosphorus and phosphorus pentachloride, see Z. angew. Chem. **40**, 973. Technically the acid is prepared by the action of 90 per cent. sulphuric acid on the vapour of trichloroethylene.

$$CCl_2 : CHCl + 2H_2O \longrightarrow CH_2Cl\cdot COOH + 2HCl.$$

The *ethyl ester*, b.p. 145°, is obtained technically by warming the readily accessible dichlorovinyl ethyl ether with water containing HCl (C. 1909, II. 78) (see p. 158):

$$CHCl : CCl\cdot OEt + H_2O \longrightarrow CH_2Cl\cdot COOEt + HCl.$$

The *chloride*, $CH_2Cl\cdot COCl$, b.p. 106°, is obtained by distilling the addition product of HCl with dichlorovinyl ethyl ether (D.R.P. 222194, C. 1910, I. 1999):

$$CH_2Cl\cdot CCl_2\cdot OEt \longrightarrow CH_2Cl\cdot COCl + EtCl.$$

The sodium and silver salts of chloroacetic acid, on the application of heat, yield polyglycollide.

When monochloroacetic acid is heated with alkalis or water, the chlorine is replaced by the hydroxyl group, and hydroxyacetic acid or glycollic acid is formed (*q.v.*). Amino-acetic acid, or glycocoll, results when the monochloro-acid is digested with ammonia.

Bromide, b.p. 127°; *anhydride*, m.p. 46°, b.p. 110°/11 mm. (Ber. **27**, 2949); *amide*, m.p. 116°, b.p. 224–225°; *nitrile*, b.p. 124°.

Dichloroacetic acid, $CHCl_2CO_2H$, b.p. 190–191°, is produced when chloral is heated with potassium cyanide or ferrocyanide and some water. If alcohol replace the water, dichloroacetic esters are formed (Ber. **10**, 2124: J. pr. Chem. [2], **88**, 531):

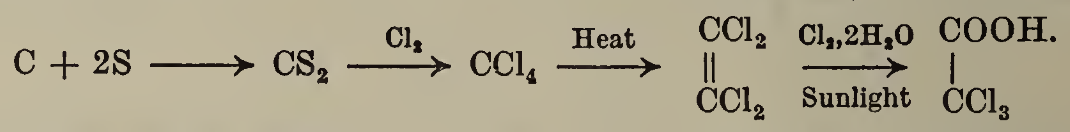
$$CCl_3CHO + H_2O + KCN = CHCl_2CO_2H + KCl + HCN.$$

Dichloroacetic acid can also be obtained by the reduction of trichloroacetic acid in benzene solution by means of copper.

When its silver salt is boiled with a little water, glyoxylic acid (*q.v.*) is produced.

Methyl ester, b.p. 142–144°; *ethyl ester*, b.p. 158°; *anhydride*, b.p. 214–216° (decomp.); *chloride*, b.p. 107–108°, formed by the autoxidation of trichloroethylene (J. pr. Chem. [2], **85**, 78); *amide*, m.p. 98°, b.p. 234°; *nitrile*, b.p. 113°.

Trichloroacetic acid, CCl_3CO_2H, m.p. 55°, b.p. 195°, the officinal *Acidum trichloraceticum*, was first prepared by *Dumas* (1839) when he allowed chlorine to act in the sunlight on acetic acid (Ann. **32**, 101). *Kolbe* (1845) made the acid by the oxidation of chloral with concentrated nitric acid (Ann. **54**, 183), and demonstrated how it could be prepared synthetically from its elements:



$$C + 2S \longrightarrow CS_2 \xrightarrow{Cl_2} CCl_4 \xrightarrow{Heat} \begin{array}{c} CCl_2 \\ \| \\ CCl_2 \end{array} \xrightarrow[\text{Sunlight}]{Cl_2,2H_2O} \begin{array}{c} COOH. \\ | \\ CCl_3 \end{array}$$

The carbon disulphide resulting from carbon and sulphur is converted by the chlorine into carbon tetrachloride, which on the application of heat becomes converted into perchloroethylene, $CCl_2{=}CCl_2$ (p. 124), and it, in turn, by the action of chlorine and water, aided by sunlight, yields trichloroacetic acid. This was the first synthesis of acetic acid, for *Melsens* had previously shown that potassium amalgam in aqueous solution reduced trichloroacetic acid to acetic acid (p. 301).

Boiling with water decomposes trichloroacetic acid into chloroform (p. 290) and CO_2, whilst excess of alkali produces formic acid and a carbonate (Ann. **342**, 122). Electrolysis gives rise to the formation of perchloroacetic trichloromethyl ester (C. 1897, II. 475).

The *methyl ester*, b.p. 152·5°; *ethyl ester*, b.p. 164°, are obtained from the acid and alcohols (Ber. **29**, 2210; C. 1901, II. 1333). *Trichloroacetyl chloride*, (*Perchloroacetaldehyde*), b.p. 118°, is formed when ozonized air or SO_3 (Ann. **308**,

324) acts on perchloroethylene (Ber. **27**, R. 509) (comp. synthesis of trichloroacetic acid from CS_2); *bromide*, b.p. 143°; *anhydride*, b.p. 224°; *amide*, m.p. 141°, b.p. 239°; *nitrile*, b.p. 83°; *trichloromethyl ester*, $CCl_3{\cdot}CO_2CCl_3$, m.p. 34°, b.p. 192° (Ann. **273**, 61).

Monobromoacetic acid, $CH_2Br{\cdot}CO_2H$, m.p. 50–51°, b.p. 208°; *ethyl ester*, b.p. 159°; *chloride*, b.p. 134°; *bromide*, $CH_2Br{\cdot}COBr$, b.p. 150°; *anhydride*, b.p. 245°; *amide*, m.p. 91°; *nitrile*, b.p. 148–150° (Ber. **38**, 2694).

Dibromoacetic acid, $C_2H_2Br_2O_2$, m.p. 54–56°, b.p. 232–235°; *ethyl ester*, b.p. 192°; *bromide*, $CHBr_2{\cdot}COBr$, b.p. 194°; *amide*, m.p. 156° (Ber. **38**, 2695); *nitrile*, b.p. 68°/24 mm.

Tribromoacetic acid, CBr_3CO_2H, m.p. 135°, b.p. 246° with decomposition, results from the interaction of perbromoethylene and nitric acid (Ann. **308**, 324). Boiling water or alkali decomposes it similarly to trichloroacetic acid (see above). *Ethyl ester*, b.p. 225°; *bromide*, b.p. 220–225°; *amide*, m.p. 120–121°; *nitrile*, b.p. 170°, is a dark red liquid, which HCl changes to the polymeric *trinitrile*, m.p. 129° (Ber. **27**, R. 730).

Moniodoacetic acid, CH_2ICO_2H, m.p. 82° (C. 1901, I. 665).

Di-iodoacetic acid, $CHI_2{\cdot}CO_2H$, m.p. 110°.

Tri-iodoacetic acid, m.p. 150°. The last two compounds have been obtained from malonic acid and iodic acid (Ber. **26**, R. 597). (Comp. iodoform, p. 291.)

Monofluoroacetic acid, $CH_2F{\cdot}COOH$, m.p. 33°, b.p. 165°, is obtained by the hydrolysis of its *methyl ester*, b.p. 104°, which in turn is prepared from methyl iodo-acetate and mercury or silver fluoride.

Difluoroacetic acid, CHF_2COOH, b.p. 134°, is prepared by oxidation of difluoroethyl alcohol (from difluoroethyl bromide). In these compounds the fluorine atom is held relatively firmly in the molecule (Jahresb. 1896, 759; C. 1903, II. 709).

Dibromofluoroacetic acid, $CBr_2F{\cdot}COOH$, m.p. 26°, b.p. 198°; *ethyl ester*, b.p. 173°, possesses a camphor-like odour; *fluoride*, $CBr_2F{\cdot}COF$, b.p. 75°, is formed from symmetrical (?) dibromodifluoroethylene by the absorption of oxygen (C. 1898, II. 702).

Substitution Products of Propionic Acid

The α-monohaloid propionic acids contain an asymmetric carbon atom; hence their esters, for example, are known in an active form. They are prepared according to the methods 4*a* and 5 (p. 331). The β-monohalogen acids are derived from acrylic acid by method 2 (p. 331), and β-iodopropionic acid from glyceric acid by method 4*a*.

α-Chloropropionic acid, $CH_3CHClCO_2H$, b.p. 186°; *ethyl ester*, b.p. 146°; *chloride*, 109–110°; *amide*, 80°; *nitrile*, b.p. 121–122°, is prepared from acetaldehyde cyanohydrin and PCl_5 (Ber. **34**, 4049).

α-Bromopropionic acid, m.p. 24·5°, b.p. 205°, is resolved into its optically active components by cinchonine; *ethyl ester*, b.p. 162°; *bromide*, b.p. 153° (Ann. **280**, 247); *anhydride*, b.p. 120°/5 mm. (Ber. **27**, 2949). Dextro-rotatory α-chloro- and α-bromopropionic esters are obtained from sarcolactic acid (Ber. **28**, 1293).

α-Iodopropionic acid, m.p. 45°, is prepared from propionyl chloride and iodine chloride (Ber. **36**, 4392).

β-Chloropropionic acid, $CH_2ClCH_2CO_9H$, m.p. 41·5°, b.p. 203–204°; *methyl ester*, b.p. 156°; *ethyl ester*, b.p. 162°; *chloride*, b.p. 143–145°.

β-Bromopropionic acid, m.p. 61·5°; *ethyl ester*, b.p. 69–70°/10 mm.; *bromide*; b.p. 154–155°.

β-Iodopropionic acid, m.p. 82°; *methyl ester*, b.p. 188°; *ethyl ester*, 202°; *amide*, m.p. 100° (Ber. **21**, 24, 97), is formed by boiling the ester with sodium amalgam and subsequently hydrolysing the mercury dipropionic acid, $Hg(CH_2{\cdot}CH_2COOH)_2$, formed, consisting of prisms, which are only slightly poisonous. The aqueous solution, when boiled, deposits a heavy precipitate of hydroxymercury propionic anhydride,  $\overline{OHgCH_2CH_2CO}$ (Ber. **40**, 386).

Dihalogen Propionic Acids.—αα-Acids are prepared by the chlorination and bromination of propionic acid (Ber. **18**, 235), or by the action of phosphorus halides on pyruvic acid; αβ-acids, by the addition of chlorine and bromine to acrylic acid, by the addition of a halogen acid to α-halogen acrylic acids, and by the oxidation of the corresponding alcohols (p. 332); ββ-acids, by the addition of a halogen acid to β-halogen acrylic acids.

αα-Dichloropropionic acid, $CH_3CCl_2CO_2H$, b.p. 185–190°; *ethyl ester*, b.p. 156–157°; *chloride*, from pyroracemic acid and PCl_5, b.p. 105–115°; *amide*, m.p. 116° (Ber. **11**, 388); *nitrile*, b.p. 105° (Ber. **9**, 1593).

The silver salt breaks down into pyroracemic acid and αα-dichloropropionic acid when heated in aqueous solution.

αα-Dibromopropionic acid, m.p. 61°, b.p. 220°; *ethyl ester*, b.p. 190°, is decomposed by sodium hydroxide into pyroracemic acid, $CH_3COCOOH$, and bromoacrylic acid (Ann. **342**, 130).

αβ-Dichloropropionic acid, $CH_2ClCHClCO_2H$, m.p. 50°, b.p. 210°; *ethyl ester*, b.p. 184°.

αβ-Dibromopropionic acid, m.p. 51° and 64°, b.p. 227° with partial decomposition, exists in two allotropic modifications, which can be readily converted one into the other, and of which the more stable possesses the higher melting point. Water or sodium hydroxide produces from it α-bromoacrylic and glyceric acids (Ann. **342**, 135): *ethyl ester*, b.p. 211–214°.

ββ-Dibromopropionic acid, m.p. 71°, is formed from β-bromoacrylic acid and HBr (Ber. **27**, R. 257).

Substitution Products of the Butyric Acids

α-Chloro-*n*-butyric acid, $CH_3CH_2CHClCO_2H$, b.p. 101°/15 mm. (Ann. **319**, 358), is a thick liquid: *ethyl ester*, b.p. 158°; *chloride*, b.p. 131°, is obtained from butyryl chloride (Ann. **153**, 241); *nitrile*, b.p. 142°.

α-Bromobutyric acid, b.p. 215°, is prepared from butyric acid.

β-Chloro-*n*-butyric acid, $CH_3CHCl{\cdot}CH_2COOH$, b.p. 99°/12 mm., is obtained from allylcyanide, and from solid crotonic acid and HCl; *nitrile*, b.p. 175°.

β-Bromo-*n*-butyric acid, m.p. 18°, b.p. 122°/16 mm., and **β-iodo-*n*-butyric acid**, m.p. 110° (Ber. **22**, R. 741; C. 1905, I. 24) have been obtained from crotonic acid and from allylcyanide.

γ-Chloro-*n*-butyric acid, $CH_2ClCH_2CH_2CO_2H$, m.p. 16°, b.p. 115°/13 mm., is obtained from the nitrile and from trimethylene carboxylic acid and HCl (Ann. **319**, 363). Trimethylene chlorobromide, $CH_2Cl{\cdot}CH_2CH_2Br$ and KCN yield *γ-Chlorobutyric nitrile*, b.p. 189° (Ann. **319**, 360). Alkali hydroxides convert the nitrile into trimethylene carboxylic acid nitrile (Vol. II) (C. 1908, I. 1357). The acid is obtained from this, and when distilled at 200° it yields HCl and butyrolactone.

γ-Bromo- and **γ-iodobutyric** acids, m.p. 33° and 41°, result from butyrolactone (*q.v.*) by the action of HBr and HI (Ber. **19**, R. 165).

αβ-Dichlorobutyric acid, $CH_3CHClCHClCO_2H$, m.p. 63°. **αβ-Dibromobutyric acid**, m.p. 85°. Both are obtained from crotonic acid (p. 344). **βγ-Dibromobutyric acid** is obtained from vinylacetic acid (p. 345).

ααβ-Trichlorobutyric acid, $CH_3{\cdot}CHCl{\cdot}CCl_2{\cdot}CO_2H$, m.p. 60°, appears in the oxidation of butyl chloral (*q.v.*) and by the action of chlorine on chlorocrotonic acids (Ber. **28**, 2661).

ααβ-Tribromobutyric acid, m.p. 115°. The solutions of the sodium salts of both acids break down, when warmed, into CO_2, sodium halide, and αα-dichloro- and αα-dibromopropylene (Ber. **28**, 2663).

α-Bromo*iso*butyric acid, $(CH_3)_2CBr{\cdot}COOH$, m.p. 48°, b.p. 199°; *ethyl ester*, b.p. 164°; *anhydride*, m.p. 63° (Ber. **27**, 2951); *amide*, m.p. 148°, with bromine and alkali (comp. p. 263) yields acetone (C. 1905, I. 1220). *α-Bromo*iso*butyryl bromide*, b.p. 163°, is converted by zinc into dimethylketen (p. 271).

α-Iodo*iso*butyric acid, m.p. 73° (C. 1900, I. 960), is prepared from *iso*butyryl chloride, S_2Cl_2, and iodine.

Halogen Substitution Products of the Higher Fatty Acids

Acids, containing the group $(CH_3)_2CH$, have their methine hydrogen substituted by chlorine when the reaction takes place in sunlight at 100° (C. 1897, II. 1100: 1899, II. 963). Among the higher members some α-bromo-acids are prepared by bromination with or without the presence of phosphorus (Ber. **25**, 486). Such compounds can also be obtained by the addition of the halogen acids or the halogen to unsaturated acids (Ann. **319**, 357: C. 1901, I. 93, 665). Dialkyl bromoacetic acids, $R_2CBrCOOH$, can also be prepared from dialkylmalonic acids by heating with bromine and water. Some of their amides are employed as soporifics (C. 1906, II. 1694).

The dibromo-addition-products of the unsaturated acids have been exhaustively studied. Water almost invariably causes the elimination of CO_2 from the $\alpha\beta$-dibromides with the formation of brominated hydrocarbons, etc., whereas CO_2 is never split off from the $\beta\gamma$- and $\gamma\delta$-derivatives, but the first products are brominated lactones, from which hydroxy-lactones and γ-ketonic acids are simultaneously obtained (Ann. **268**, 55).

B. OLEFINE MONOCARBOXYLIC ACIDS (OLEIC ACID SERIES), $C_nH_{2n-1}CO_2H$

The acids of this series, bearing the name Oleic Acid Series because oleic acid belongs to them, differ from the saturated fatty acids by containing two atoms of hydrogen less than the latter. They also bear the same relation to them that the alcohols of the allyl series do to the normal alcohols. We can consider them as being derivatives of the olefines, C_nH_{2n}, produced by the replacement of one atom of hydrogen by the carboxyl group.

Some of the methods employed for the preparation of the unsaturated acids are similar to those used with the saturated acids. Others correspond with the methods used with the olefines, and others, again, are peculiar to this class of bodies.

They are formed *from compounds containing the same number of carbon atoms*:

(1) Like the saturated fatty acids, by the oxidation of their corresponding alcohols and aldehydes; thus, allyl alcohol and its aldehyde afford acrylic acid:

$$\underset{\text{Allyl alcohol.}}{CH_2:CH{\cdot}CH_2OH} \longrightarrow \underset{\text{Acrolein.}}{CH_2:CH{\cdot}CHO} \longrightarrow \underset{\text{Acrylic acid.}}{CH_2:CH{\cdot}CO_2H}.$$

(2) By the action of alcoholic potassium hydroxide (p. 333) on the monohalogen derivatives of the fatty acids, or by the action of heat on them, together with a tertiary base such as diethylaniline or quinoline (C. 1898, I. 778).

$$\underset{\alpha\text{-Chlorobutyric acid.}}{CH_3{\cdot}CH_2{\cdot}CHCl{\cdot}CO_2H} \text{ and } \underset{\beta\text{-Chlorobutyric acid.}}{CH_3{\cdot}CHCl{\cdot}CH_2{\cdot}CO_2H} \text{ yield } \underset{\text{Crotonic acid.}}{CH_3{\cdot}CH:CH{\cdot}CO_2H}$$

The β-derivatives are especially reactive, sometimes parting with halogen acids when boiled with water (p. 333), whereas the γ-halogen acids yield hydroxy-acids and lactones.

(3) The $\alpha\beta$-derivatives of the acids (p. 336) readily lose two halogen atoms, (*a*) either by the action of nascent hydrogen—

$$\underset{\alpha\beta\text{-Dibromopropionic acid.}}{CH_2Br{\cdot}CHBr{\cdot}CO_2H} + 2H = \underset{\text{Acrylic acid.}}{CH_2:CH{\cdot}CO_2H} + 2HBr,$$

or (*b*) even more readily when heated with a solution of potassium iodide, in which instance the primary di-iodo-compounds part with iodine (p. 165):

$$CH_2I{\cdot}CHI{\cdot}CO_2H = CH_2:CH{\cdot}CO_2H + I_2.$$

(4) By the addition of hydrogen to acetylenecarboxylic acids:

$$\underset{\text{Tetrolic acid.}}{CH_3{\cdot}C \vdots C{\cdot}COOH} + 2H = \underset{\text{Crotonic acid.}}{CH_3{\cdot}CH:CH{\cdot}COOH}.$$

(5) By the removal of water (in the same manner in which the

olefines C_nH_{2n} are formed from the alcohols) from the hydroxy-fatty acids (the acids belonging to the lactic series):

$$\underset{\alpha\text{-Hydroxypropionic acid.}}{CH_3CH(OH)\cdot CO_2H} \text{ and } \underset{\beta\text{-Hydroxypropionic acid.}}{CH_2(OH)\cdot CH_2\cdot CO_2H} \text{ yield } \underset{\text{Acrylic acid.}}{CH_2:CH\cdot CO_2H}.$$

Here again the β-derivatives are most inclined to alteration, losing water when heated. The removal of water from α-derivatives is best accomplished by treating the esters with PCl_3. The esters of the unsaturated acids are formed first, and can be saponified by means of alkalis. Another method is to act with P_2O_5 on the nitriles of the hydroxy-acids (C. 1898, II. 662). β-Hydroxy-acids also yield olefine carboxylic acids when boiled with alkalis (Ann. **283**, 58).

If both α-situated hydrogen atoms in a β-hydroxy-acid are substituted, warming the ester with P_2O_5 causes elimination of water in the βγ position; if, however, there is no hydrogen in the γ position, an internal rearrangement occurs which favours the expulsion of water (C. 1906, II. 317, 318):

$$CH_3CH(OH)C(CH_3)CO_2R \xrightarrow{-H_2O} CH_2:CHC(CH_3)_2CO_2R$$

$$CH_2(OH)C(CH_3)_2CO_2R \xrightarrow{-H_2O} CH(CH_3):C(CH_3)CO_2R.$$

This reaction is the reverse of the pinacone-pinacolin transformation (*q.v.*).

(6) Amino-fatty acids lose the amino-group, after previous exhaustive methylation (p. 198), and yield olefine carboxylic acids (Ber. **33**, 1408).

(7) α-Alkyl-α-bromosuccinic acids lose HBr and CO_2 when boiled with sodium hydroxide (C. 1899, I. 1071).

Nucleus-synthetic Methods.—(8) Some may be prepared synthetically from the halogen derivatives, $C_nH_{2n-1}X$, through the cyanides (p. 324); thus, allyl iodide yields allyl cyanide and crotonic acid: the position of the double bond is changed at the same time:

$$CH_2:CHCH_2I \longrightarrow CH_2:CH\cdot CH_2CN \longrightarrow CH_3CH:CHCO_2H.$$

The replacement of the halogen by CN in the compounds $C_nH_{2n-1}X$ is conditioned by the structure of the latter. Although allyl iodide, $CH_2:CH\cdot CH_2I$, yields a cyanide, chloroethylene, $CH_2:CHCl$, and β-chloropropylene, $CH_3\cdot CCl:CH_2$, are not capable of this reaction.

(9) The action of CO_2 and magnesium on an ethereal solution of allyl bromide produces vinyl acetic acid (Ber. **36**, 2897):

$$CH_2:CHCH_2Br + Mg + CO_2 = CH_2:CHCH_2COOMgBr.$$

(10) Some acids have been synthetically prepared by Perkin's reaction, which is readily brought about with benzene derivatives, but proceeds with difficulty in the fatty series. It consists in treating the aldehydes with a mixture of acetic anhydride and sodium acetate (comp. Cinnamic acid):

$$\underset{\text{Œnanthol.}}{C_6H_{13}CHO} + CH_3\cdot CO_2Na = \underset{\text{Nonenoic acid.}}{C_6H_{13}CH:CH\cdot CO_2Na} + H_2O.$$

(Ann. **277**, 79: C. 1899, I. 595).

β-Dimethylacrylic acid is obtained from acetone, malonic acid and acetic anhydride (Ber. **27**, 1574).

Pyroracemic acid acts analogously with sodium acetate—carbon dioxide splits off and crotonic acid results (Ber. **18**, 987).

A modification of this method consists in allowing the aldehyde, dissolved in anhydrous ether to react with malonic acid in the presence of anhydrous pyridine at a suitable temperature (Bull. Soc. Chim. **41**, 440).

Methods of formation, dependent upon the breaking-down of long carbon chains:

(11) By the decomposition of *unsaturated β-ketonic acids*, syn-

thetically prepared by the introduction of unsaturated radicals into acetoacetic esters. Allyl acetoacetic ester yields allylacetic acid (p. 347).

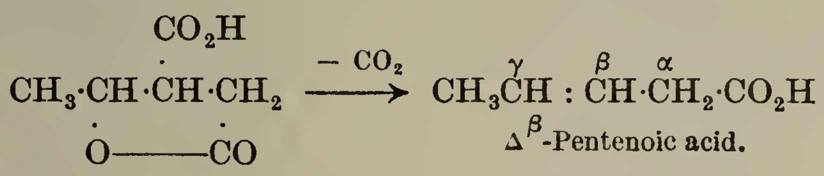
(12) By the decomposition of *unsaturated malonic acids*, containing the two carboxyl groups attached to the same carbon atom (p. 564):

$$\underset{\text{Ethylidenemalonic acid.}}{CH_3{\cdot}CH : C(CO_2H)_2} = \underset{\text{Crotonic acid.}}{CH_3{\cdot}CH : CH{\cdot}CO_2H} + CO_2.$$

A large number of unsaturated acids have been prepared by Adams and his co-workers from the corresponding unsaturated substituted malonic acids (J.A.C.S. **52**, 1281).

(13) $\beta\gamma$-Unsaturated acids are prepared by distilling γ-lactone-β-carboxylic acids, the alkylated paraconic acids (Ber. **23**, R. 91). In the same manner $\gamma\delta$-unsaturated acids result from the δ-lactone-γ-carboxylic acids (Ber. **29**, 2367):

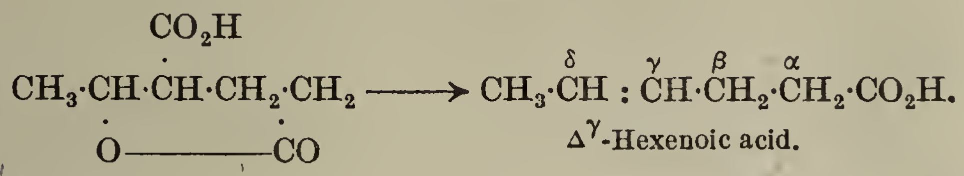
Methyl Paraconic acid.



$$\begin{array}{l} \qquad\quad CO_2H \\ CH_3{\cdot}CH{\cdot}CH{\cdot}CH_2 \\ \qquad O\text{———}CO \end{array} \xrightarrow{-CO_2} CH_3\overset{\gamma}{C}H : \overset{\beta}{C}H{\cdot}\overset{\alpha}{C}H_2{\cdot}CO_2H$$

Δ^{β}-Pentenoic acid.

δ-Caprolactone--carboxylic acid.



$$\begin{array}{l} \qquad\qquad\quad CO_2H \\ CH_3{\cdot}CH{\cdot}CH{\cdot}CH_2{\cdot}CH_2 \\ \qquad O\text{—————}CO \end{array} \longrightarrow CH_3{\cdot}\overset{\delta}{C}H : \overset{\gamma}{C}H{\cdot}\overset{\beta}{C}H_2{\cdot}\overset{\alpha}{C}H_2{\cdot}CO_2H.$$

Δ^{γ}-Hexenoic acid.

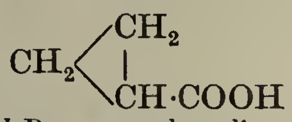
Isomerism.—An isomer of acrylic acid is neither known nor possible. The second member of the series has three structurally isomeric, open-carbon chain modifications:

$$(1)\ CH_3{\cdot}CH{=}CH{\cdot}CO_2H;\quad (2)\ CH_2{=}CH{\cdot}CH_2{\cdot}CO_2H;\quad (3)\ CH_2{=}C{<}^{CO_2H}_{CH_3}.$$

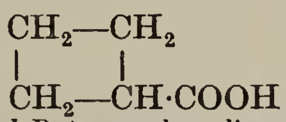
There are actually four unsaturated acids of the formula $C_4H_6O_2$. To vinylacetic acid and methacrylic acid are assigned respectively the formulæ 2 and 3, on the evidence of their methods of preparation. This leaves the formula 1 to represent both crotonic acids, and their isomerism must be explained as a stereochemical one (*cis-trans* isomerism, see p. 41).

Numerous pairs of unsaturated acids are known, which are stereochemically related to each other in the same way as the two crotonic acids, *e.g.* angelic and tiglic acids, oleic and elaidic acids, erucic and brassidic acids.

The monocarboxylic acids of the *cyclo*paraffins are structurally isomeric with the unsaturated acids. Thus, *cyclo*propanecarboxylic acid is isomeric with the unsaturated acids C_3H_5COOH and *cyclo*butanecarboxylic acid with the acids C_4H_7COOH:



*cyclo*Propanecarboxylic acid.



*cyclo*Butanecarboxylic acid.

Properties and Reactions.—The unsaturated acids, which resemble the saturated acids in their general behaviour, differ from them in their unsaturated character, as shown by their capacity to form addition compounds. They thus combine the properties of a fatty acid with those of an olefine. The $\alpha\beta$-unsaturated acids in particular very readily form addition products. For dissociation constants of the unsaturated acids, see Ann. **334**, 201: **348**, 256.

(1) *Reduction.*—The unsaturated acids are converted by reduction into the corresponding fatty acid.

The lower members usually combine with 2H produced by the action of zinc on dilute sulphuric acid, while the higher members remain unaffected. Sodium amalgam apparently only reduces the $\alpha\beta$-unsaturated acids. By heating with hydriodic acid and phosphorus or by the action of hydrogen in the presence of a nickel, platinum or palladium catalyst, all unsaturated acids are reduced, the $\alpha\beta$-unsaturated compounds being again, in general, the most readily attacked (Ber. **41**, 1476, 2273 : **42**, 1325).

(2) Esters of the unsaturated acids, such as acrylic and crotonic acids, polymerize under the influence of sodium methoxide, whereby the double bond is broken, and the β-carbon atom of one molecule joins the α-carbon atom of a second, accompanied by the migration of a hydrogen atom :

$$2CH_2 : CH{\cdot}COOH = CO_2H{\cdot}C(: CH_2){\cdot}CH_2{\cdot}CH_2{\cdot}COOH.$$

(3) They combine with halogen acids, forming monohalogen fatty acids. In so doing the halogen atom enters the molecule as far as possible from the carboxyl group (p. 331).

(4) They unite with the halogens to form dihalogen fatty acids (J.C.S. **97**, 2450).

All these reactions have already been given as methods for forming fatty acids and their halogen derivatives.

The addition of halogen to the unsaturated acids is used for the purpose of separating the unsaturated from the saturated acids (C. 1921, IV. 1239).

(5) Ammonia converts the olefine carboxylic acids into amino-fatty acids : crotonic acid yields β-aminobutyric acid (*cf.* C. 1909, II. 1988). Hydrazine and phenylhydrazine behave similarly with the same compounds.

(6) Diazoacetic ester and diazomethane combine with the olefine carboxylic esters to produce pyrazolinecarboxylic esters : acrylic ester and diazoacetic ester yield 3 : 4-pyrazolinecarboxylic ester (*q.v.*) (*Buchner*, Ann. **273**, 222).

(7) The olefinecarboxylic acids unite with N_2O_4, forming dinitro-carboxylic acids (*cf.* Addition of N_2O_4 to olefines, p. 104) :

$$CH_3CH : CHCOOH \xrightarrow{N_2O_4} CH_3CH(NO_2){\cdot}CH{\cdot}(NO_2)COOH.$$

These addition compounds are destroyed when heated with fuming hydrochloric acid with the formation of mono- and dicarboxylic acids, *e.g.* :

$$CH_3(CH_2)_7CH(NO_2){\cdot}CH(NO_2){\cdot}(CH_2)_7COOH \longrightarrow \underset{\text{Pelargonic acid.}}{CH_3(CH_2)_7COOH} + \underset{\text{Azelaic acid.}}{COOH{\cdot}(CH_2)_7{\cdot}COOH}.$$

These reactions are of value in determining the position of the double bond in unsaturated acids (J. pr. Chem. [2] **86**, 521).

(8) The behaviour of unsaturated acids towards *alkalis* is note-worthy.

(*a*) When heated to 100°, with KOH or NaOH, they frequently absorb the elements of water and pass into hydroxy acids. Thus, from acrylic acid we obtain lactic acid :

$$CH_2 : CH{\cdot}CO_2H + H_2O = CH_3{\cdot}CH(OH){\cdot}CO_2H.$$

(*b*) $\beta\gamma$-Unsaturated acids rearrange themselves to $\alpha\beta$-unsaturated acids (*Fittig*, Ann. **283**, 47, 269 : Ber. **28**, R. 140) when they are boiled with alkali hydroxide :

$$\overset{\epsilon}{C}H_3\cdot\overset{\delta}{C}H_2\cdot\overset{\gamma}{C}H=\overset{\beta}{C}H\cdot\overset{\alpha}{C}H_2\cdot COOH \longrightarrow \overset{\epsilon}{C}H_3\cdot\overset{\delta}{C}H_2\cdot\overset{\gamma}{C}H_2\cdot\overset{\beta}{C}H=\overset{\alpha}{C}H\cdot COOH.$$

Hydrosorbic acid. *n*-Butylideneacetic acid.

In general, a distant double bond migrates nearer the COOH-group (*cf.* Oleic acid, Monatsh. **38,** 1).

(*c*) When fused with potassium or sodium hydroxide their double union is severed and two monobasic fatty acids result :

$$CH_2 : CH\cdot CO_2H + 2H_2O = CH_2O_2 + CH_3\cdot CO_2H + H_2.$$

Acrylic acid. Formic acid. Acetic acid.

$$CH_3CH : CH\cdot CO_2H + 2H_2O = CH_3\cdot CO_2H + CH_3\cdot CO_2H + H_2.$$

Crotonic acid. Acetic acid. Acetic acid.

The decomposition occasioned by fusion with alkalis is not a reaction which can be applied in ascertaining constitution, because under the influence of the alkalis there may occur a displacement or rearrangement of the double union.

(9) *Oxidation.*—Oxidizing agents like chromic acid, nitric acid and potassium permanganate have the same effect as alkalis. (*a*) The group linked to carboxyl is usually further oxidized, and thus a dibasic acid results.

(*b*) When carefully oxidized with permanganate, the unsaturated acids undergo an alteration similar to that of the olefines and dihydroxy acids are formed (*Fittig*, Ber. **21**, 1887).

$$CH_3\cdot CH : C(C_2H_5)CO_2H + O + H_2O = CH_3CH(OH)\cdot C(OH)(C_2H_5)CO_2H.$$

α-Ethyl crotonic acid. αβ-Dihydroxy-α-ethylbutyric acid.

By the oxidation of the methyl or ethyl esters with permanganate in hot acetone or acetic acid solution, the unsaturated acids can be converted into the mono- and dibasic acids obtainable by rupture of the double bond in high yield, and without shift of the ethylenic linkage. This method is of value in the determination of the constitution of such unsaturated acids (Armstrong and Hilditch, J.S.C.I. **44,** 43T).

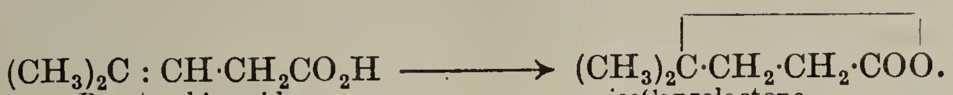
(10) Ozone produces *ozonides* by action on the olefine carboxylic acids. They are decomposed by water into aldehydes and aldehyde-acids, a reaction which indicates their constitution (comp. p. 106) (Ann. **343**, 34 : **374,** 356) :

$$CH_3\cdot CH : CHCOOH + O_3 + H_2O = CH_3CHO + HOC\cdot COOH + H_2O_2.$$

Crotonic (or *iso*crotonic) acid. Acetaldehyde. Glyoxylic acid.

The unsaturated acids resemble olefines in their reaction with perbenzoic acid (Ber. **42,** 4811 : see also p. 106).

(11) βγ-Unsaturated acids when heated with dilute sulphuric acid yield γ-lactones :



$$(CH_3)_2C : CH\cdot CH_2CO_2H \longrightarrow (CH_3)_2C\cdot CH_2\cdot CH_2\cdot COO.$$

Pyroterebic acid. *iso*Caprolactone.

As the αβ-unsaturated acids are usually unaffected by this procedure, it forms a method for the separation of αβ- and βγ-unsaturated acids (Ann. **283,** 51 : *cf.*, however, Ber. **42,** 4710).

(12) Many αβ-unsaturated esters react with the sodium derivative of ethyl malonate to form saturated tricarboxylic esters (*Michael condensation*). This reaction has recently been shown to be reversible, an equilibrium being attained between the unsaturated ester and malonic ester and the addition product (Ingold and Powell, J.C.S. **119**, 1976).

Acrylic acid [Propene-acid], $CH_2 : CH{\cdot}CO_2H$, m.p. 7°, b.p. 141°, is obtained according to the general methods :

(1) From β-chloro-, β-bromo-, or β-iodo-propionic acid by the action of alcoholic potassium hydroxide or lead oxide.

(2) From αβ-dibromopropionic acid by the action of zinc and sulphuric acid, or potassium iodide, or reduced copper containing iron (C. 1900, II. 173).

(3) By heating β-hydroxypropionic acid (hydracrylic acid).

The best method consists in oxidizing acrolein with silver oxide, or by the conversion of acrolein, by successive treatment with hydrochloric and nitric acid, into β-chloropropionic acid, and the subsequent decomposition of this acid by alkali hydroxide (Ber. **26**, R. 777 : Ber. **34**, 573).

Acrylic acid is a liquid with an odour like that of acetic acid, and is miscible with water. If allowed to stand for some time, it is transformed into a solid polymer. By protracted heating on the water-bath with zinc and sulphuric acid it is converted into propionic acid, a reaction which does not occur in the cold. It combines with bromine to form αβ-dibromopropionic acid, and with the halogen acids to yield β-substitution products of propionic acid (p. 335). If fused with alkali hydroxides, it is broken up into acetic and formic acids.

The *silver salt*, $C_3H_3O_2Ag$, consists of shining needles ; *lead salt*, $(C_3H_3O_2)_2Pb$, crystallizes in long, silky, glistening needles ; *ethyl ester*, $C_3H_3O_2{\cdot}C_2H_5$, b.p. 101°, obtained from the ester of αβ-dibromopropionic acid by means of zinc and sulphuric acid, is a pungent-smelling liquid ; *methyl ester*, b.p. 85°, is polymerized by sodium methoxide to α-methylene glutaric ester (Ber. **34**, 427).

Acryl chloride, $CH_2 : CH{\cdot}COCl$, b.p. 75° ; *anhydride* $[CH_2 : CH{\cdot}CO]_2O$, b.p. 97°/35 mm. ; *amide*, $CH_2 : CH{\cdot}CONH_2$, m.p. 84° ; *nitrile, vinyl cyanide*, $CH_2 : CH{\cdot}CN$, b.p. 78° (Ber. **26**, R. 776 : C. 1899, II. 662).

Substitution Products.—There are two isomeric forms of mono- and di-substituted acrylic acids.

α-Chloroacrylic acid, $CH_2 : CCl{\cdot}CO_2H$, m.p. 64°, results when αβ- and also αα-dichloropropionic acids are heated with alcoholic potassium hydroxide. It combines with HCl at 100° to produce αβ-dichloropropionic acid (Ber. **10**, 1499 : **18**, 244).

β-Chloroacrylic acid, $CHCl : CH{\cdot}CO_2H$, m.p. 84°, is produced together with dichloroacrylic acid in the reduction of chloralide with zinc and hydrochloric acid (Ann. **203**, 83 : **239**, 263), also from propiolic acid, $CH \vdots C{\cdot}CO_2H$ (p. 351), by the addition of HCl. It unites with HCl to ββ-dichloropropionic acid. *Ethyl ester*, b.p. 146°.

α-Bromoacrylic acid, m.p. 69–70°, is slowly decomposed by alkalis into acetylene and alkali bromide and bicarbonate (Ann. **342**, 135).

β-Bromoacrylic acid, m.p. 115–116°.

β-Iodoacrylic acid, is known in two modifications, m.ps. 139–140° and 65° (Ber. **19**, 542).

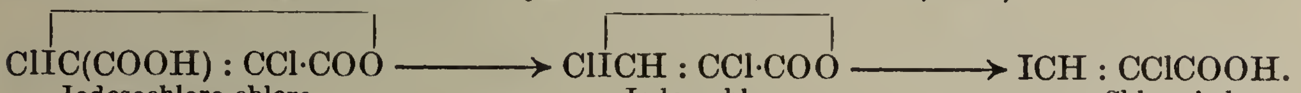
αβ-Dichloroacrylic acid, m.p. 87° ; *ββ-dichloroacrylic acid*, m.p. 76–77°.

αβ-Dibromoacrylic acid, m.p. 85–86° ; *ββ-dibromoacrylic acid*, m.p. 86°.

αβ-Di-iodoacrylic acid, m.p. 106° ; *ββ-di-iodoacrylic acid*, m.p. 133° (Ber. **18**, 2284).

α-Chloro-β-iodoacrylic acid, m.p. 89°, results from reduction of *iodosochloro-*

acrylic acid, or its iodosochloride, which in turn is prepared by the action of water or alcohol on *iodosochloro-chlorofumaric acid* (Ann. **369**, 120).



$$\mathrm{ClIC(COOH):CCl{\cdot}COO} \longrightarrow \mathrm{ClICH:CCl{\cdot}COO} \longrightarrow \mathrm{ICH:CClCOOH.}$$

Iodosochloro-chloro-fumaric acid. Iodosochloro-chloroacrylic acid. Chloro-iodo-acrylic acid.

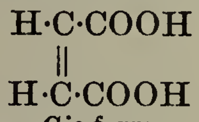
Trichloroacrylic acid, m.p. 76° ; *ethyl ester*, b.p. 193° ; *orthoethyl ester*, $\mathrm{CCl_2:CClC(OC_2H_5)_3}$, b.p. 236°, from hexachloropropylene (Ann. **297**, 312).

Tribromoacrylic acid, m.p. 117–118°.

Butenoic Acids, $C_4H_6O_2$

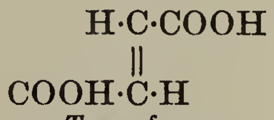
The four-carbon members of the olefinic acids comprise the two crotonic acids, vinylacetic acid and methacrylic acid.

Crotonic Acids.—As already mentioned, the isomerism of the two crotonic acids is to be attributed to the different spatial arrangements of the groups in the two acids, the two forms being represented by the following formulæ :



$$\begin{array}{c}\mathrm{H{\cdot}C{\cdot}COOH}\\ \|\\ \mathrm{H{\cdot}C{\cdot}COOH}\end{array}$$

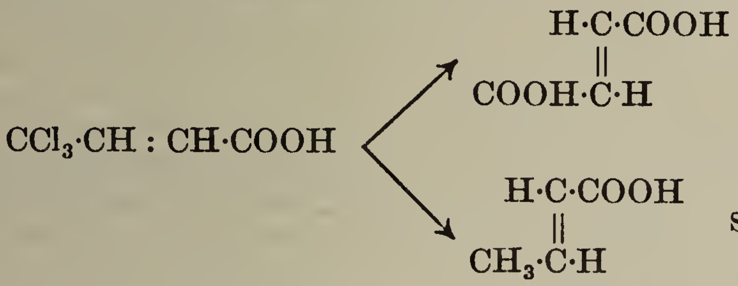
Cis-form
(Plane-symmetrical).



$$\begin{array}{c}\mathrm{H{\cdot}C{\cdot}COOH}\\ \|\\ \mathrm{COOH{\cdot}C{\cdot}H}\end{array}$$

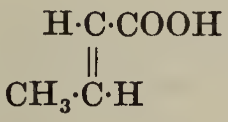
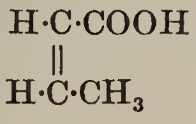
Trans-form
(Axial-symmetrical).

The assigning of spatial formulæ to the isomeric olefinic acids presents very considerable difficulties, and the formulæ originally ascribed to the two crotonic acids has not stood the test of recent experimental work. Auwers has synthesized a $\gamma\gamma\gamma$-trichlorocrotonic acid which can be smoothly converted at 0° into fumaric acid, which is known to possess the *trans*-configuration, and by reduction into solid crotonic acid. As these reactions should not affect the double linking, it is concluded that the trichloro acid, and therefore the solid crotonic acid is to be represented by the *trans*-configuration and *iso*crotonic acid by the *cis*-formula (Ber. **56**, 715) :



$$\mathrm{CCl_3{\cdot}CH:CH{\cdot}COOH} \begin{array}{l}\nearrow \begin{array}{c}\mathrm{H{\cdot}C{\cdot}COOH}\\ \|\\ \mathrm{COOH{\cdot}C{\cdot}H}\end{array} \quad \text{Fumaric acid.}\\ \searrow \begin{array}{c}\mathrm{H{\cdot}C{\cdot}COOH}\\ \|\\ \mathrm{CH_3{\cdot}C{\cdot}H}\end{array} \quad \text{Solid crotonic acid.}\end{array}$$

The melting and boiling points of crotonic and *iso*crotonic acids and their halogen derivatives is given in the following table.

Trans-**Configuration**		M.P.	B.P.
Crotonic acid	 $\begin{array}{c}\mathrm{H{\cdot}C{\cdot}COOH}\\ \|\\ \mathrm{CH_3{\cdot}C{\cdot}H}\end{array}$	72°	180°
α-Chlorocrotonic acid		99°	212°
β-Chlorocrotonic acid		94°	200°
γ-Chlorocrotonic acid		77°	—
α-Bromocrotonic acid		106°	—
β-Bromocrotonic acid		95°	—
Cis-**Configuration**			
*iso*Crotonic acid	 $\begin{array}{c}\mathrm{H{\cdot}C{\cdot}COOH}\\ \|\\ \mathrm{H{\cdot}C{\cdot}CH_3}\end{array}$	15°	75°/23mm.
α-Chloro*iso*crotonic acid		66°	—
β-Chloro*iso*crotonic acid		59°	195°
α-Bromo*iso*crotonic acid		92°	—

1. **Ordinary or solid crotonic acid** is obtained according to the general methods of formation (pp. 337–339):

(1) by the oxidation of crotonaldehyde, $CH_3CH : CH{\cdot}CHO$ (p. 254);

(2) by the action of alcoholic potassium hydroxide on α-bromobutyric acid and β-iodobutyric acid;

(3) by the action of KI on αβ-dibromobutyric acid;

(4) by the distillation of β-hydroxybutyric acid;

(5) by the hydrolysis of allyl cyanide, $CH_2 : CHCH_2CN$, from allyl iodide and potassium cyanide, accompanied by shift of the double linkage (Ber. **21**, R. 494: C. 1903, II. 657).

(6) Crotonic acid is most readily prepared by condensing malonic acid with acetaldehyde in the presence of pyridine (see p. 543) or by heating malonic acid, $CH_2(CO_2H)_2$, with paraldehyde and acetic anhydride: the ethylidene-malonic acid first produced decomposes into CO_2 and crotonic acid (Ann. **218**, 147);

(7) Finally, from *iso*crotonic acid, dissolved in water or carbon bisulphide, by the action of a trace of bromine, in sunlight.

Crotonic acid crystallizes in fine, woolly needles or in large plates, and dissolves in 12 parts water at 20°. The warm aqueous solution reduces alkaline silver solutions with the formation of a silver mirror. Zinc and sulphuric acid, but not sodium amalgam, convert it into normal butyric acid. It combines with HBr and HI to yield β-bromo- and β-iodobutyric acid, and with chlorine and bromine to form αβ-dichloro- and αβ-dibromobutyric acids. Its methyl ester combines at 180° with sulphur (Ber. **28**, 1636).

It polymerizes under the influence of sodium ethoxide to form α-ethylidene-β-methyl glutaric ester (Ber. **33**, 3323). Crotonic ethyl ester, similarly treated, yields β-ethoxybutyric ester (Ber. **33**, 3329). When fused with potassium hydroxide, crotonic acid breaks up into two molecules of acetic acid; nitric acid oxidizes it to acetic and oxalic acids, and potassium permanganate to dihydroxybutyric acid (Ann. **268**, 7), which can be resolved by means of its quinidine salt (C. 1904, I. 788, 934). Similarly to *iso*crotonic acid, crotonic acid is split up by ozone and water into acetaldehyde and glyoxylic acid (p. 455).

By the action of ultra-violet irradiation crotonic acid, and more readily its amide, is partially isomerized into *iso*crotonic acid or its amide (Ber. **47**, 1786).

Methyl ester, b.p. 121°: *chloride*, b.p. 114° (Ber. **34**, 191): *anhydride*, b.p. 128–130°/19 mm., from crotonic acid and acetic anhydride, gives, with BaO_2, *crotonyl peroxide* $(CH_3CH : CHCO)_2O_2$, m.p. 41° (C. 1903, I. 958): *amide*, m.p. 159° (Ber. **47**, 1789): *anilide*, m.p. 118°.

α-**Chlorocrotonic acid**, $CH_3{\cdot}CH : CCl{\cdot}CO_2H$, is obtained when trichlorobutyric acid (p. 336) is treated with zinc and hydrochloric acid, or zinc dust and water, or when αβ-dichlorobutyric acid (m.p. 63°) is heated with pyridine. The last reaction probably involves the intermediate formation of α-chloro*iso*crotonic acid, which is then transposed by the action of the pyridine hydrochloride into the *trans*-chloro acid (Ber. **43**, 3039).

β-Chlorocrotonic acid, $CH_2{\cdot}CCl : CH{\cdot}CO_2H$, is obtained in small quantities (together with β-chloro*iso*crotonic acid) from acetoacetic ester by the action of PCl_5 and water and by the addition of HCl to tetrolic acid. With boiling alkalis it yields tetrolic acid (p. 352). Sodium amalgam converts both α- and β-chlorocrotonic acids into ordinary crotonic acid.

γ-Chlorocrotonic acid, $CH_2Cl{\cdot}CH : CH{\cdot}CO_2H$, m.p. 77°; from the *nitrile*, b.p. 73°/15 mm., which is prepared by distilling the addition product of HNC and epichlorhydrin with P_2O_5 (C. 1900, II. 37).

α-**Bromocrotonic acid**, m.p. 106°, is obtained from αβ-dibromobutyric acid (m.p. 85°) by heating with pyridine (Ber. **43**, 3042).

β-Bromocrotonic acid, m.p. 95°, is obtained from tetrolic acid (p. 352).

Dichloro- and *dibromocrotonic acids*, see tetrolic acid, p. 352.

γγγ-**Trichlorocrotonic acid**, m.p. 114°, b.p. 146°/18 mm., is formed by heating trichlorohydroxybutyric acid with sodium acetate and acetic anhydride (Ber. **46**, 490) and is converted by concentrated sulphuric acid in the cold into fumaric acid, and by reduction into solid crotonic acid (Ber. **56**, 715).

(2) *iso***Crotonic acid**, *quartenylic acid*, cis-*crotonic acid*, *allocrotonic acid*, m.p. 15°, was first obtained from β-chloro*iso*crotonic acid by means of sodium

amalgam, and is also formed from α-chloro*iso*crotonic acid. It is also formed by distilling β-hydroxyglutaric acid under reduced pressure (C. 1898, II. 1011).

Heated in a closed tube to 170–180°, it is converted into crotonic acid, a change which also partially occurs during distillation, or by the action of bromine on an aqueous or carbon bisulphide solution in sunlight (C. 1897, II. 259). The reverse change from crotonic to *iso*crotonic acid takes place partially under the influence of ultra-violet light (Ber. **47**, 1786).

It can be separated from the solid crotonic acid by means of the greater solubility of its sodium salt in alcohol, or its more easily soluble quinine salt. (C. 1897, II. 260 : 1904, I. 167). Melted with potassium hydroxide *iso*crotonic acid yields only acetic acid, like the ordinary crotonic acid, into which it may first be changed. Sodium amalgam has no action on it. It absorbs HI, forming β-iodobutyric acid (Ber. **22**, R. 741). Chlorine unites with it to form a liquid dichloride, $C_4H_6Cl_2O_2$, the *iso*-αβ-dichlorobutyric acid, which gives up HCl, changing into α-chlorocrotonic acid. $KMnO_4$ oxidizes it to a dihydroxybutyric acid (*q.v.*) (Ann. **228**, 16). *Anilide*, m.p. 102°.

α-**Chloro*iso*crotonic acid** is obtained by the action of sodium hydroxide on αβ-dichlorobutyric acid. It is the most soluble of the four chlorocrotonic acids (Ber. **22**, R. 52). Under the action of pyridine hydrochloride, it is changed into chlorocrotonic acid (*q.v.*).

β-*Chloro*iso*crotonic acid* (with β-chlorocrotonic acid) is produced by the action of PCl_5 and water on acetoacetic ester, $CH_3CO·CH_2COC_2H_5$. It is very probable that β-dichlorobutyric acid is formed at first, and this afterward parts with HCl. It is also formed by protracted heating of β-chlorocrotonic acid.

Sodium amalgam converts both the α- and β-chloro*iso*crotonic acids into liquid *iso*crotonic acid (Ber. **22**, R. 52).

α- **Bromo*iso*crotonic acid** is produced by the action of sodium hydroxide on free αβ-dibromobutyric acid (Ber. **21**, R. 242).

(3) **Vinylacetic acid,** $CH_2 : CH·CH_2COOH$, b.p. 71°/13 mm., is produced together with glutaconic acid, by heating β-hydroxyglutaric acid ; also from β-bromoglutaric acid by the action of sodium hydroxide solution ; or by heating a solution of its neutral sodium salt. . It can further be obtained from allyl bromide, CO_2, and Mg, in ether (Ber. **36**, 2897). It is an oil, volatile in steam. Boiling with sodium hydroxide converts it into ordinary crotonic acid and β-hydroxybutyric acid ; acids produce the ordinary crotonic acid only. Bromine changes it into βγ-dibromobutyric acid, which gives β-hydroxy-γ-butyrolactone when boiled with water. *Calcium salt*, $(C_4H_5O_2)_2Ca + H_2O$ (Ber. **35**, 938).

Vinylacetonitrile, allyl cyanide, $CH_2 : CH·CH_2CN$, b.p. 118°, obtained from allyl bromide or iodide with alkali cyanide, or from γ-chlorobutyronitrile and pyridine (C. 1921, III. 30), yields solid crotonic acid on hydrolysis, accompanied by internal change. Bromine produces βγ-dibromobutyronitrile which, on saponification, yields βγ-dibromobutyric acid ; reduction of the latter with zinc and alcohol gives rise to vinylacetic acid (C. 1905, I. 434). *Anilide*, m.p. 58°.

(4) **Methacrylic acid,** $CH_2 : CMe·COOH$, m.p. 16°, b.p. 160·5°. Its ethyl ester was first obtained by the action of PCl_3 on hydroxy*iso*butyric ester, $(CH_3)_2·C(OH)·CO_2·C_2H_5$. It can be prepared from α-bromo*iso*butyric acid by warming it with concentrated sodium hydroxide solution (Ann. **342**, 159). It is, however, best prepared by boiling *citra*-bromopyrotartaric acid (from citraconic acid and HBr) with water or a sodium carbonate solution :

$$C_5H_7BrO_4 = C_4H_6O_2 + CO_2 + HBr.$$

It crystallizes in prisms which are readily soluble in water ; it polymerizes on keeping and in contact with HCl to *polymethacrylic acid* (Ber. **30**, 1227). Sodium amalgam easily converts it into *iso*butyric acid. With HBr and HI it forms α-bromo- and α-iodo-*iso*butyric acid, whilst bromine produces αβ-dibromo-*iso*butyric acid, whereby the above constitution is substantiated (J. pr. Chem. [2] **25**, 369). Fusion with potassium hydroxide decomposes it into propionic and formic acids. The *nitrile*, b.p. 90°, is produced from acetone cyanhydrin by P_2O_5 (C. 1898, II. 662). *Anilide*, m.p. 87°.

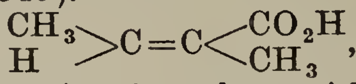
Bromomethacrylic acid and iso*bromomethacrylic acid*, $BrCH : C(CH_3)COOH$, m.ps. 64° and 66°, are produced from *citra*- and *mesa*-dibromopyrotartaric acid. They are separated from one another by means of petroleum ether. Heat changes the *iso*-acid into the normal form, which on further heating is decomposed into HBr, CO_2, and allene (p. 114) (Ann. **343**, 163).

The characterization of the four butenoic acids can be effected through their anilides, $C_3H_5{\cdot}CO{\cdot}NHC_6H_5$, which are obtained by treating the acids with PCl_5, aniline, and sodium hydroxide (Ber. **38**, 254):

Crotonic anilide, m.p. 118°; *vinylacetic anilide*, m.p. 58°; iso*crotonic anilide*, m.p. 102°; *methacrylic anilide*, m.p. 87°.

Pentenoic Acids, $C_4H_7{\cdot}CO_2H$

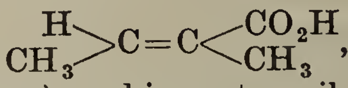
Of the isomers of this formula, angelic or αβ-dimethylacrylic acid is the most important. It bears the same relation to tiglic acid as crotonic does to *iso*crotonic acid (p. 343).

Angelic acid  $\genfrac{}{}{0pt}{}{CH_3}{H}{>}C{=}C{<}\genfrac{}{}{0pt}{}{CO_2H}{CH_3}$, (Spatial configuration, Ber. **56**, 723), m.p. 45°, b.p. 185°, exists free along with valeric and acetic acids in the roots of *Angelica archangelica*, and as butyl and amyl esters, together with tiglic amyl ester, in Roman oil of cumin, the oil of *Anthemis nobilis*.

Angelic acid congeals, when well cooled, and may be thus separated from liquid valeric acid by pressure. Angelic and tiglic acids can be separated by means of the calcium salts, that of the first being very readily soluble in cold water (Ber. **17**, 2261: Ann. **283**, 105).

When angelic acid is boiled for twenty hours with sodium hydroxide, two-thirds of it is converted into tiglic acid. Heating with water at 120° will change over one-half of it to tiglic acid (Ann. **283**, 108). When pure angelic acid is heated to boiling for hours it is completely changed to tiglic acid. The same occurs by the action of concentrated sulphuric acid at 100°. It dissolves without difficulty in hot water, and volatilizes readily in steam.

Ethyl ester, b.p. 141°.

Tiglic acid, *α-methylcrotonic acid*,  $\genfrac{}{}{0pt}{}{H}{CH_3}{>}C{=}C{<}\genfrac{}{}{0pt}{}{CO_2H}{CH_3}$, m.p. 64·5°, b.p. 198° present in Roman oil of cumin (see above), and in croton oil (from *Croton tiglium*), which is a mixture of glycerol esters of various fatty and oleic acids. It can be prepared from α-hydroxy-α-methylbutyric acid, $C_2H_5{\cdot}CMe(OH){\cdot}CO_2H$, by the abstraction of water. Together with angelic acid it is obtained from hydroxypivalic acid, $HO{\cdot}CH_2C{\cdot}(CH_3)_2COOH$, by an internal change accompanied by the loss of water, according to mode of formation 5 (p. 337). Also from acetaldehyde and propionic acid, by mode of formation 10 (p. 338). It is converted by bromine into two *dibromides* (Ann. **250**, 240: **259**, 1: **272**, 1: **273**, 127: **274**, 99). For their constitution, compare Ber. **24**, R. 668. *Ethyl ester*, b.p. 152°.

The three possible acids, $C_4H_7CO_2H$, with normal structure are also known (Fittig, Ann. **283**, 47: Ber. **27**, 2658).

Propylideneacetic acid, *Δ^{α}-pentenoic acid*, $CH_3{\cdot}CH_2{\cdot}CH : CH{\cdot}CO_2H$, m.p. 10°, b.p. 201°, is formed, together with γ-hydroxyvaleric acid, on boiling ethylidenepropionic acid with sodium hydroxide; as well as from malonic acid, propionic aldehyde and acetic anhydride, together with Δ^{β}-pentenoic acid; *dibromide*, m.p. 56°.

Ethylidenepropionic acid, *Δ^{β}-pentenoic acid*, $CH_3CH : CH{\cdot}CH_2CO_2H$, b.p. 194°, is best prepared by the distillation of methylparaconic acid (Ber. **37**, 1997). It is also produced by the reduction of vinylacrylic acid (p. 353) by sodium amalgam (Ber. **35**, 2320); *dibromide*, m.p. 65°.

α-Ethylacrylic acid, $CH_2{=}C(C_2H_5)COOH$, m.p. 45°, b.p. 180°, is obtained from α-bromo-α-ethylsuccinic acid. On warming with concentrated sulphuric acid it is partially changed to tiglic acid, partially into CO and methyl ethyl ketone, $CH_3{\cdot}CO{\cdot}C_2H_5$ (C. 1905, I. 591). Sulphuric acid produces similar decompositions and changes in the homologous α-alkylacrylic acids (C. 1905, II. 612).

ββ-Dimethylacrylic acid, $(CH_3)_2C : CH{\cdot}CO_2H$, m.p. 70°, is obtained (1) from β-hydroxy-*iso*valeric acid by distillation; (2) from acetone and malonic acid by means of acetic anhydride (Ber. **27**, 1574); (3) from its ester, produced when α-bromo*iso*valeric acid ester is heated with diethylaniline (Ann. **280**, 252); (4) from mesityl oxide by the breaking-down action of sodium hypochlorite:

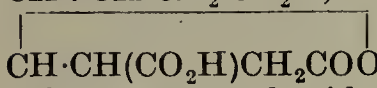
$$(CH_3)_2C : COCH_3 \xrightarrow{NaClO} (CH_3)_2C : CHCOOH + CHCl_3.$$

(C. 1905, II. 614.) The ethyl ester and HNO_3 yield two isomeric mononitro compounds. See Ber. **29**, R. 956 for its derivatives.

Allylacetic acid, *Δ^{γ}-pentenoic acid*, $CH_2 : CH\cdot CH_2\cdot CH_2\cdot CO_2H$, b.p. 187°, is obtained on heating allylmalonic acid.

Hexenoic Acids, $C_6H_{10}O_2$

Hydrosorbic acid, *Propylidenepropionic acid*, *Δ^{β}-Hexenoic acid*, $CH_3\cdot CH_2\cdot CH : CH\cdot CH_2\cdot CO_2H$, b.p. 208°, is obtained from ethylparaconic acid, $CH_3\cdot CH_2\cdot$



$CH\cdot CH(CO_2H)CH_2COO$, according to method 13 (p. 339); hence it is probably a $\beta\gamma$-unsaturated acid. It is the first reduction product of sorbic acid, $CH_3CH : CH\cdot CH : CH\cdot CO_2H$, the two hydrogen atoms attaching themselves in accord with Thiele's rule in the $\alpha\delta$-position at each end of the conjugated system, with formation of a new $\beta\gamma$-double bond. When hydrosorbic acid is heated with sodium hydroxide, the isomeric *iso*hydrosorbic acid is produced with shift of the double bond.

***iso*Hydrosorbic acid**, *Δ^{α}-Hexenoic acid*, $CH_3(CH_2)_2CH : CH\cdot COOH$, m.p. 33°, b.p. 216°, is also obtained, together with a little of the Δ^{β}-acid by heating α-bromocaproic ester with quinoline (Ber. **24**, 83 : **27**, 1998). When its bromine addition product is boiled with water, hydroxy-caprolactone and homolævulinic acid result (Ann. **268**, 69).

Δ^{γ}-Hexenoic acid, $CH_3CH : CH\cdot CH_2COOH$, m.p. 0°, b.p. 206° (see mode of formation 13, p. 339). Permanganate breaks it down into acetic acid and succinic acid (Ber. **37**, 1999).

Δ^{δ}-Hexenoic acid, $CH_2 : CHCH_2CH_2CH_2COOH$, b.p. 203°, is formed, together with the $\gamma\delta$-acid, from α-hydroxy-α-methyladipic acid by the action of heat; also from ϵ-aminocaproic acid by means of nitrous acid (Ber. **37**, 1999).

Vinyldimethylacetic acid, $CH_2 : CH\cdot C(CH_3)_2COOH$, b.p. 185°. Its ester is obtained from $\alpha\alpha\beta$-trimethylhydracrylic ester by P_2O_5. The acid is oxidized by permanganate to dimethylmalonic acid, $(CH_3)_2C(COOH)_2$. Analogously many homologous *alkenyldimethylacetic acids* can be obtained (C. 1906, II. 317, 1116). Their dibromides are partially decomposed by alkalis in an abnormal manner.

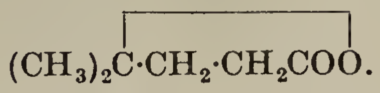
***Δ^{α}-iso*Hexenoic acid**, *β-isoPropylacrylic acid*, $(CH_3)_2CH\cdot CH : CHCOOH$, b.p. 212°, from β-hydroxycaproic acid or α-bromo*iso*caproic ester (Ber. **29**, R. 667 : C. 1899, I. 1157).

β-Methyl-Δ^{β}-pentenoic acid, $CH_3\cdot CH : CMe\cdot CH_2\cdot COOH$, b.p. 199°, is obtained according to method 13 (p. 339).

β-Methyl-Δ^{α}-pentenoic acid, $CH_3\cdot CH_2\cdot CMe : CH\cdot COOH$, m.p. 46°, b.p. 207° (Ber. **42**, 4707).

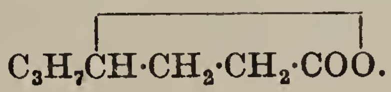
Ethylcrotonic acid, $CH_3\cdot CH : C(C_2H_5)COOH$, m.p. 40°, and **ethyl*iso*crotonic acid**, b.p. 200°, are obtained together on the distillation of diethylglycollic acid, $(C_2H_5)_2C(OH)\cdot COOH$. The first is a sublimable solid, the second a liquid. The latter is converted into the solid acid when heated under pressure to 200° (Ann. **334**, 105). The *calcium salt* of the *iso*-acid is less soluble in hot water than in cold.

Pyroterebic acid, $(CH_3)_2C : CH\cdot CH_2\cdot CO_2H$, and **teracrylic acid**, $C_3H_7\cdot CH : CH\cdot CH_2\cdot CO_2H$, b.p. 218° (Ann. **208**, 37, 39), belong to the acids $C_6H_{10}O_2$ and $C_7H_{12}O_2$. They deserve notice because of their genetic connection with two oxidation products of turpentine oil—terebic acid and terpenylic acid—which will be considered in Vol. II. Pyroterebic acid is changed by protracted boiling or by HBr to the isomeric *iso*caprolactone:



$$(CH_3)_2C\cdot CH_2\cdot CH_2COO.$$

Teracrylic acid is converted by HBr into the isomeric heptolactone:



$$C_3H_7CH\cdot CH_2\cdot CH_2\cdot COO.$$

Higher Unsaturated Acids

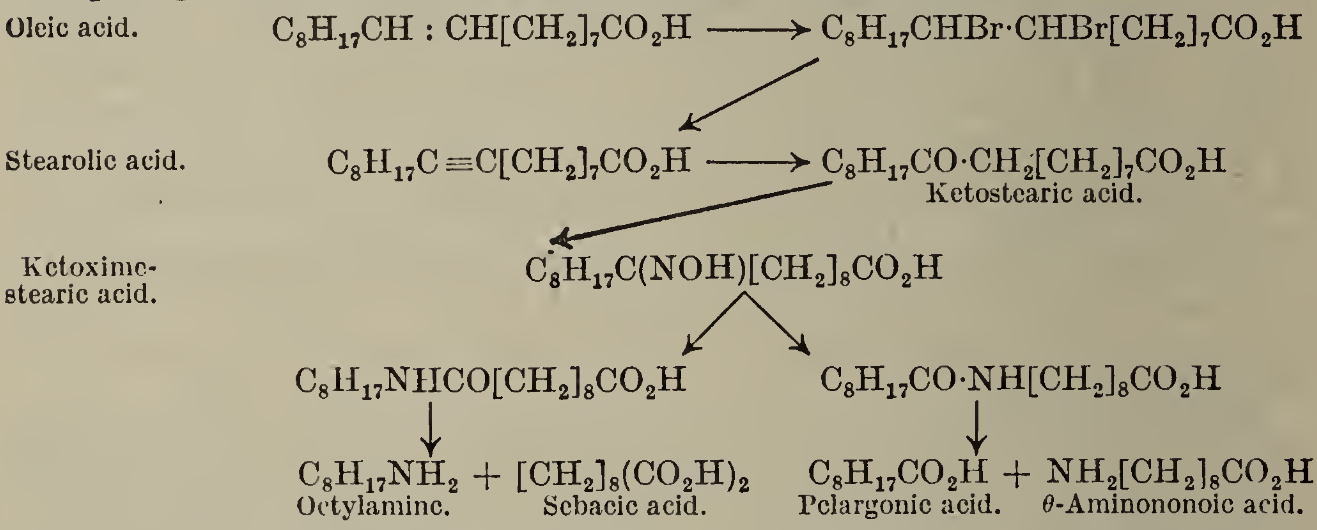
Nonenoic acid, $CH_3(CH_2)_5CH : CH{\cdot}COOH$, b.p. 144°/13 mm. from œnanthal according to methods 10 and 12 (J.C.S. **97**, 299).

Δ^{α}-Decenoic acid, $CH_3(CH_2)_6CH : CH{\cdot}COOH$, is obtained from hexy paraconic acid according to method 13. **Δ^{θ}-Decenoic acid,** $CH_2 : CH[CH_2]_7{\cdot}COOH$, b.p. 142°/4 mm., occurs in small amount in butter (Ber. **55**, 2197).

Δ^{ι}-Undecenoic acid, $CH_2{=}CH(CH_2)_8CO_2H$, m.p. 24·5°, b.p. 165°/15 mm., is produced, together with œnanthol (p. 238) (C. 1901, I. 612) by distilling castor oil under reduced pressure. It yields sebacic acid, $(CH_2)_8(CO_2H)_2$ (*q.v.*), on oxidation (Ber. **19**, R. 338 : **19**, 2224). *Chloride*, b.p. 128°/14 mm. ; *anhydride*, m.p. 13°, b.p. 170°/11 mm. ; *nitrile*, b.p. 130°/14 mm. (Ber. **33**, 3580) ; *amide*, m.p. 85° (Ber. **31**, 2349). When its *dibromide*, m.p. 38°, is incompletely decomposed by alcoholic potassium hydroxide, *dehydro-undecylenic acid*, $CH{\equiv}C[CH_2]_8{\cdot}CO_2H$, m.p. 43°, is obtained, which, fused at 180° with potassium hydroxide, changes to *undecolic acid*, $CH_3{\cdot}C \vdots C[CH_2]_7CO_2H$, m.p. 59° (Ber. **29**, 2232).

Δ^{α}-Dodecenoic acid, $CH_3{\cdot}[CH_2]_8{\cdot}CH : CH{\cdot}COOH$, m.p. 13–14°, b.p. 186–189°/12 mm., is obtained by method 2 (p. 337) (J.C.S. **1931**, 2046).

To ascertain the point of the doubly linked carbon atoms in the higher olefine monocarboxylic acids, the latter may be converted into their corresponding acetylene monocarboxylic acids (p. 350), which, in turn, are oxidized and split open at the point of triple carbon union ; or they are changed to ketonecarboxylic acids, and these are then broken down. Thus, oleic acid yields *stearolic acid*, which may be oxidized to *azelaic acid*, $C_7H_{14}(CO_2H)_2$, and *pelargonic acid*, $C_8H_{17}CO_2H$. This would mean that in stearolic acid the carbon atoms 9 and 10 are united by three bonds, and that they are the atoms which in oleic acid are in double union. This conclusion is confirmed by the conversion of stearolic acid, by means of concentrated sulphuric acid, into *ketostearic acid*, whose oxime undergoes the *Beckmann rearrangement* at 400°, as the result of the action of concentrated sulphuric acid. Two acid amides result, which are decomposed by fuming hydrochloric acid, the one into octylamine and sebacic acid, the other into pelargonic acid and θ-aminononoic acid (Ber. **27**, 172) :



Oleic acid. $C_8H_{17}CH : CH[CH_2]_7CO_2H \longrightarrow C_8H_{17}CHBr{\cdot}CHBr[CH_2]_7CO_2H$

Stearolic acid. $C_8H_{17}C{\equiv}C[CH_2]_7CO_2H \longrightarrow C_8H_{17}CO{\cdot}CH_2[CH_2]_7CO_2H$ Ketostearic acid.

Ketoxime-stearic acid. $C_8H_{17}C(NOH)[CH_2]_8CO_2H$

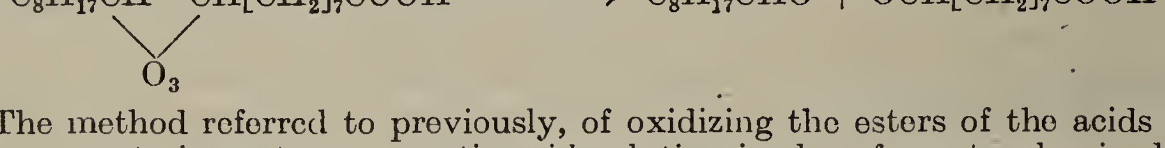
$C_8H_{17}NHCO[CH_2]_8CO_2H$ $\quad$ $C_8H_{17}CO{\cdot}NH[CH_2]_8CO_2H$

$C_8H_{17}NH_2 + [CH_2]_8(CO_2H)_2$ $\quad$ $C_8H_{17}CO_2H + NH_2[CH_2]_8CO_2H$

Octylamine. Sebacic acid. Pelargonic acid. θ-Aminononoic acid.

The constitution of hypogæic and erucic acids has been determined in the same manner.

The constitution of stearolic acid still remained doubtful, however, since ketostearic acid, $C_{18}H_{17}CO[CH_2]_8COOH$, could also be formed from an acid of the formula $C_7H_{15}C{\equiv}C[CH_2]_8COOH$. However, the assumed constitution of oleic acid is substantiated by boiling its ozonide with water, whereby the decomposition products, nonyl aldehyde and azelaic aldehyde acid, were obtained together with their oxidation products, pelargonic acid and azelaic acid (Ber. **39**, 3732) :

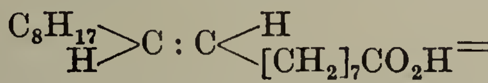


$$\underbrace{C_8H_{17}CH{-}CH}_{O_3}[CH_2]_7COOH \longrightarrow C_8H_{17}CHO + OCH[CH_2]_7COOH$$

The method referred to previously, of oxidizing the esters of the acids with permanganate in acetone or acetic acid solution is also of great value in determining the position of the double bond (see p. 341).

Palmitoleic acid (*Zoomaric acid*), $CH_3[CH_2]_5CH : CH[CH_2]_7COOH$, occurs in whale oil (J.S.C.I. **44**, 180T).

Hypogæic acid, $CH_3[CH_2]_7CH : CH[CH_2]_5CO_2H$, m.p. 33°, b.p. 236°/15 mm, found as glycerol ester in earthnut oil (from the fruit of *Arachis hypogœa*), crystallizes in needles. It results when stearolic acid is fused with KOH at 200° (Ber. **27**, 3397).

Oleic acid,  $\begin{matrix}C_8H_{17}\\H\end{matrix}\!\!>C : C<\!\!\begin{matrix}H\\ [CH_2]_7CO_2H\end{matrix}=C_{18}H_{34}O_2$, m.p. 14°, b.p. 223°/10 mm., occurs as glycerol ester (*triolein*) in nearly all fats, especially in the oils, as olive oil, almond oil, cod-liver oil, etc. It is obtained in large quantities as a by-product in the manufacture of stearic acid (p. 306). Synthesis, see J.C.S. **127**, 175.

In preparing oleic acid, olive or almond oil is saponified with potassium hydroxide and the aqueous solution of the potassium salts precipitated with lead acetate. The lead salts which separate are dried and extracted with ether, when lead oleate dissolves, leaving as insoluble the lead salts of all other fatty acids. The ethereal solution is mixed with hydrochloric acid, the lead chloride is filtered off, and the liquid is concentrated. The acid obtained in this way may be fractionated by distillation under greatly diminished pressure.

Oleic acid in a pure condition is odourless, and does not redden litmus. On exposure to the air it oxidizes, becomes yellow, and acquires a rancid odour. Nitric acid oxidizes it with formation of all the lower fatty acids from capric to acetic, and at the same time dibasic acids, like sebacic acid, are produced. A permanganate solution (J.S.C.I. **44,** 43T) oxidizes it with the formation of pelargonic acid (p. 306) and azelaic acid (p. 562): by oxidation, two stereoisomeric *dihydroxystearic acids*, m.pp. 95° and 136° are formed (J.C.S. **1926,** 1828. Stereochemical relationships of these two acids, see Annual Reports, 1926, **23,** 99 : 1927, **24,** 86 : 1928, **25,** 83). When oleic acid is heated with potassium hydroxide at 220°, a migration of the double bond to the $\alpha\beta$- position, followed by loss of two carbon atoms and the formation of palmitic acid takes place (C. 1915, I. 934). Attempts to assign space-formulæ to oleic and elaidic acids, see Rec. Trav. Chim. **45,** 914.

It unites with bromine to form liquid dibromostearic acid, $C_{18}H_{34}Br_2O_2$, which is converted by alcoholic KOH into *monobromooleic acid*, $C_{19}H_{33}BrO_2$, and then into stearolic acid (p. 352). Reduction by hydrogen and finely-divided nickel (C. 1903, I. 1199), or by electrolytic methods (C. 1905, II. 305) converts oleic acid into stearic acid.

Oleic anhydride, m.p. 22° (Ber. **57,** 99); *chloride,* b.p. 213°/13 mm. (Ber. **33,** 3584).

Elaidic acid,  $\begin{matrix}C_8H_{17}\\H\end{matrix}\!\!>C:C<\!\!\begin{matrix}[CH_2]_7CO_2H\\H\end{matrix}$, m.p. 51°, b.p. 225°/10 mm., results from the action of nitrous acid on oleic acid. It is also obtained when oleic acid is heated with water and sulphur at 180° (Ber. **62,** 2712). Oxidation with alkaline permanganate produces a *dihydroxystearic acid,* m.p. 99° (C. 1899, I. 1068).

Bromide, m.p. 27°. *Chloride,* b.p. 216°/13 mm. *Anhydride,* m.p. 50°. *Nitrile,* b.p. 214°/16 mm. (Ber. **33,** 3582). *Amide,* m.p. 90° (C. 1899, I. 1070).

Oleic and elaidic acids, when reduced with hydriodic acid or with hydrogen in the presence of finely-divided nickel, both yield stearic acid, this showing the presence of a straight chain of 18 carbon atoms in each. The position of the double bond in the two acids is the same as is shown by the formation of the same oxidation products, pelargonic and azelaic acids, when the two former acids are treated with ozone or permanganate (Ann. **343**, 354 : C. 1898, II. 629). Oleic and elaidic acids are therefore to be regarded as stereoisomers, bearing the same relationship to each other as crotonic to *iso*crotonic acid.

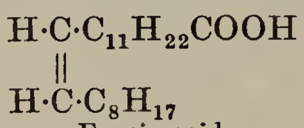
***iso*-Oleic acid**, $C_{18}H_{34}O_2$, m.p. 44–45°, is obtained from the HI-addition product of oleic acid—iodostearic acid—by treatment with alcoholic potassium hydroxide ; or from hydroxystearic acid, formed from oleic acid by the action of concentrated sulphuric acid, by distillation under reduced pressure (Ber. **21**, R. 398 : **21**, 1878 : **27**, R. 576). By the breakdown of the N_2O_4 addition product with concentrated hydrochloric acid, caprylic and sebacic acids are formed, pointing to the constitution $CH_3]CH_2]_6CH : CH[CH_2]_8COOH$ for *iso*oleic acid (J. pr. Chem. [2], **86**, 539 : *cf.* Bull. Soc. Chim. [4] **39**, 230).

Δ^{α}-Oleic acid, $CH_3[CH_2]_{14}CH{:}CHCOOH$, m.p. 59° is prepared from α-iodostearic acid and alcoholic potassium hydroxide. Potassium permanganate produces *αβ-dihydroxystearic acid*, m.p. 126°, and subsequently palmitic acid (C. 1906, I. 819).

Petroselinic acid, $CH_3[CH_2]_{10}CH : CH[CH_2]_5COOH$, m.p. 34°, occurs as glyceride in the seed of Sheep's Parsley (*Petroselinum sativum*) and gives on oxidation lauric and adipic acids (Ber. **42**, 1638 : **J.S.C.I. 46**, 174 : Rec. Trav. Chim. **46**, 492).

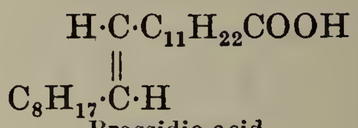
Rapic acid, $C_{18}H_{34}O_2$, occurs as glyceride in rape oil (Ber. **29**, R. 673).

Erucic and brassidic acids.



$$\begin{array}{c} H{\cdot}C{\cdot}C_{11}H_{22}COOH \\ \| \\ H{\cdot}C{\cdot}C_8H_{17} \end{array}$$

Erucic acid.



$$\begin{array}{c} H{\cdot}C{\cdot}C_{11}H_{22}COOH \\ \| \\ C_8H_{17}{\cdot}C{\cdot}H \end{array}$$

Brassidic acid.

(Space formulæ, see Gazzetta, **45**, II. 208 : Rec. Trav. Chim. **45**, 914.)

Erucic acid, m.p. 33–34°, b.p. 254·5°/10 mm., occurs as its glyceride in rapeseed oil (*Brassica campestris*), in the fatty oil of mustard seed, and in grape-seed oil. By oxidation, erucic acid yields nonylic acid and brassylic acid (Ber. **24**, 4120 : **25**, 961, 2667 : **26**, 639, 838, 1867 : R. 795, 811).

On catalytic reduction in presence of nickel, it yields behenic acid (Monatsh. **34**, 1126). *Anhydride*, m.p. 47–50° (C. 1899, I. 1070).

Brassidic acid, m.p. 66°, b.p. 256°/10 mm., is prepared from erucic acid by the action of nitrous acid (Ber. **19**, 3320) and bears the same relation to it as elaidic does to oleic acid. Its *anhydride*, m.p. 64°, is obtained from erucic anhydride and nitrous acid.

***iso*Erucic acid**, m.p. 55–57°, appears to be an inseparable mixture of Δ^{λ}- and Δ^{ν}-docosenecarboxylic acids (J.C.S. **1927**, 371).

Cetoleic acid, $CH_3[CH_2]_9CH : CH[CH_2]_9COOH$, is an isomer of erucic acid which occurs in many marine animal oils (Toyama, J.S.C.I. Japan. **30**, 597 : Brit. Chem. Abst. **1928**, A, 154).

UNSATURATED ACIDS, $C_nH_{2n-3}CO_2H$

The acids of this series contain either a trebly linked pair of carbon atoms, or two doubly linked pairs of carbon atoms, and are, therefore, distinguished as *acetylene monocarboxylic acids* (propiolic acid series) and *diolefine monocarboxylic acids*.

C. ACETYLENE CARBOXYLIC ACIDS

Methods of Formation.—(1*a*) By the action of alcoholic potassium hydroxide on the brom-addition products of the oleic acids, and (*b*) the monohalogen substitution products of the oleic acids. This is similar to the formation of the acetylenes from the dihalogen substitution products of the paraffins and the monohalogen substitution products of the olefines.

(2) From the sodium derivatives of the mono-alkylacetylenes by the action of CO_2:

$$CH_3{\cdot}C{\equiv}CNa + CO_2 = CH_3C{\equiv}C{\cdot}CO_2Na.$$

The acetylene magnesium halides (pp. 111, 112) can be used instead of the sodium derivatives (C. 1909, II. 182).

(3) Their nitriles are obtained from acetylene magnesium halides and cyanogen chloride (Bull. Soc. Chim. [4] **17**, 228).

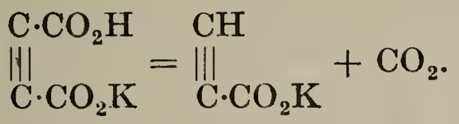
The acetylenic acids, like the acetylenes, are capable of combining with 2 or 4 monovalent atoms.

The addition of the constituents of water at the treble bond converts these substances into keto-acids. Like the β-keto-acids (*q.v.*) the $\alpha\beta$-acetylene carboxylic acids (alkylpropiolic acids) lose CO_2 on heating and become converted into acetylenes. Boiling with aqueous alkalis produces intermediate β-keto-acids, which break up into ketones and alkali carbonates (comp. C. 1903, II. 487, etc.).

Ammonia converts alkyl propiolic esters into *amides*, which give up water to phosphoric anhydride, forming *nitriles*. Primary and secondary amines when added on to the molecule form *β-amino-acrylic acids*; hydrazines form *pyrazolones*, diazoacetic ester forms *pyrazolecarboxylic esters* and azoimide *osotriazolecarboxylic esters* (see Vol. II).

A solution of sodium alcoholate or alcoholic potassium hydroxide, acting on esters or nitriles, produce derivatives of *β-alkoxyacrylic acids* or acetalcarboxylic acid, $RC(OC_2H_5):CHCOOH$ and $RC(OC_2H_3)_2{\cdot}CH_2COOH$ (C. 1904, I. 659, 1906, I. 651, 912, 1095: 1907, I. 25, 738).

Propiolic acid, *Propargylic acid* [Propyne-acid], $CH:C{\cdot}CO_2H$, m.p. 9°, b.p. 52°/18 mm. The *potassium salt*, $C_3HO_2K + H_2O$, is produced from the primary potassium salt of acetylene dicarboxylic acid, when its aqueous solution is heated; by loss of CO_2:



$$\begin{array}{l}C{\cdot}CO_2H\\ |||\\ C{\cdot}CO_2K\end{array} = \begin{array}{l}CH\\ |||\\ C{\cdot}CO_2K\end{array} + CO_2.$$

It is more conveniently prepared by the action of carbon dioxide on sodium acetylide (Ber. **59**, 1681: D.R.P. 411, 107).

The aqueous solution of the salt is precipitated by ammoniacal silver and cuprous chloride solutions, with formation of explosive metallic derivatives. By prolonged boiling with water the potassium salt is decomposed into acetylene and potassium carbonate.

Free propiolic acid, liberated from the potassium salt, is a liquid with an odour resembling that of glacial acetic acid. It dissolves readily in water, alcohol, and ether, and reduces silver and platinum salts. Exposed to sunlight out of contact with the air it polymerizes to trimesic acid:

$$3C_2H{\cdot}CO_2H = C_6H_3(CO_2H)_3.$$

Sodium amalgam converts it into propionic acid. It forms β-halogenacrylic acids with the halogen acids (p. 342) (Ber. **19**, 543), and with the halogens yields $\alpha\beta$-dihalogen-acrylic acids.

Ethyl ester, b.p. 119°. With ammoniacal cuprous chloride it unites to a stable yellow-coloured compound. Zinc and sulphuric acid reduce it to ethyl propargyl ether (p. 158) (Ber. **18**, 2271). *Amide*, m.p. 61°, yields on distillation with phosphorus pentoxide the *nitrile* (cyanoacetylene), $CH:C{\cdot}CN$, m.p. 5°, b.p. 42·5° (Compt. rend. **151**, 946).

Halogen Derivatives of Propiolic Acid.—*Chloropropiolic acid*, $CCl{\equiv}C{\cdot}CO_2H$, is produced from dichloroacrylic acid (p. 342), and bromopropiolic acid, C_3BrHO_2, from mucobromic acid. *Iodopropiolic acid*, m.p. 140°, is obtained by saponifying its *ethyl ester*, m.p. 68°, which may be prepared from the Cu compound of propiolic ester by the action of iodine.

The three acids decompose readily into carbon dioxide and spontaneously inflammable **chloroacetylene,** $CCl{\equiv}CH$, bromoacetylene and iodoacetylene. The addition of halogen acids leads to ββ-dihalogen acrylic acids, whilst the halogens give rise to trihalogen acrylic acids.

Homologous Acetylenic Acids.—Carbon dioxide converts the sodium compounds of the corresponding alkylacetylenes into the homologues of propiolic acid (Ber. **12**, 853 : J. pr. Chem. [2] **37**, 417 : Ber. **33**, 3586) : the same result is obtained with chlorocarbonic esters (C. 1901, I. 1148 : 1903, I. 824 : II. 487) :

$$RC{\equiv}CNa + ClCO_2C_2H_5 \longrightarrow RC{\equiv}CCO_2C_2H_5 + NaCl.$$

		M.P.	B.P.
Tetrolic acid, Methylacetylenecarboxylic acid	$CH_3C{\equiv}C{\cdot}CO_2H$	76°	203°
Ethylacetylenecarboxylic acid	$CH_3{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CO_2H$	80°	—
n-Propylacetylenecarboxylic acid	$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CO_2H$	27°	125° (20 mm.)
*iso*Propylacetylenecarboxylic acid	$(CH_3)_2CH{\cdot}C{\equiv}C{\cdot}CO_2H$	38°	107° (20 mm.)
n-Butylacetylenecarboxylic acid	$CH_3{\cdot}[CH_2]_3C{\equiv}C{\cdot}CO_2H$	liquid	136° (20 mm.)
tert.-Butylacetylenecarboxylic acid	$(CH_3)_3C{\cdot}C{\equiv}C{\cdot}CO_2H$	48°	110° (10 mm.)
Amylpropiolic acid	$C_5H_{11}C{\equiv}C{\cdot}CO_2H$	5°	149° (20 mm.)
Hexylpropiolic acid	$C_6H_{13}C{\equiv}C{\cdot}CO_2H$	– 10°	155° (18 mm.)
Heptylpropiolic acid	$C_7H_{15}C{\equiv}C{\cdot}CO_2H$	6–10°	166° (20 mm.)
Nonylpropiolic acid	$C_9H_{19}C{\equiv}C{\cdot}CO_2H$	30°	—
Tetradecylpropiolic acid	$CH_3[CH_2]_{13}C{\equiv}C{\cdot}CO_2H$	44°	—

Tetrolic acid has been the most thoroughly investigated, and is obtained from β-chlorocrotonic acid and β-chloro*iso*crotonic acid when these are boiled with potassium hydroxide (Ann. **345**, 103). At 210° the acid decomposes into CO_2 and allylene, C_3H_4 (Ber. **27**, R. 751). Potassium permanganate oxidizes it to acetic and oxalic acids. It combines with HCl and HBr, forming β-chlorocrotonic acid and β-bromocrotonic acid (Ber. **22**, R. 51 : **21**, R. 243). With bromine, in sunlight, it yields *dibromocrotonic acid*, m.p. 120°, whereas in the dark the halogen produces the isomeric *dibromocrotonic acid*, m.p. 94° (Ber. **28**, 1877 : **34**, 4216). ααβ-Trichlorobutyric acid (p. 336), upon the loss of HCl, yields two *dichlorocrotonic acids*, m.p. 75° and 92° (Ber. **28**, 2665). These two acids are also produced when chlorine acts on tetrolic acid.

Tetrolic ethyl ester, b.p. 164°, forms the *amide*, m.p. 148°, with ammonia, together with β-aminocrotonic ester. An aqueous solution of the amide, when heated with mercuric chloride, becomes hydrated, forming acetoacetic amide :

$$CH_3C{\equiv}CCONH_2 \longrightarrow CH_3CO{\cdot}CH_2CONH_2,$$

Phenylhydrazine forms with tetrolic ester, phenylmethylpyrazolone ; diazoacetic ester produces a pyrazole derivative (Ann. **345**, 100).

Several higher homologues of propiolic acid have been prepared by the action of alcoholic potassium hydroxide on the brom-addition products of the higher olefine monocarboxylic acids.

Undecolic acid, $CH_3C \vdots C[CH_2]_7CO_2H$, m.p. 59°, is obtained from undecenoic acid (p. 348). By oxidation, azelaic acid is formed (Ber. **33**, 3571). Isomeric with it is dehydro-undecylenic acid (p. 348).

Stearolic acid, $C_8H_{17}C \vdots C[CH_2]_7CO_2H$, m.p. 48° (constitution, see p. 348), is obtained from oleic and elaidic acids.

Behenolic acid, $C_{22}H_{40}O_2$, m.p. 57·5° (constitution, see p. 348), from the bromides of erucic and brassidic acids (Ber. **24**, 4116 : **26**, 640, 1867). On warming the last two acids with fuming nitric acid they yield the monobasic acids : *stearoxylic*, or *θι-diketostearic acid*, $CH_3[CH_2]_7CO{\cdot}CO[CH_2]_7CO_2H$, m.p. 86°, and *behenoxylic*, or *μν-diketobehenic acid*, $CH_3[CH_2]_7CO{\cdot}CO{\cdot}[CH_2]_{11}CO_2H$, m.p. 96° (Ber. **28**, 276).

Sulphuric acid converts stearolic acid into ketostearic acid, and behenolic acid into ketobrassidic acid (Ber. **26**, 1867). (Oxidation, comp. Erucic and Brassidic acids, p. 350.)

Taririnic acid, $CH_3[CH_2]_{10}C : C[CH_2]_4COOH$, m.p. 50·5°, occurs as glyceride as a principal ingredient in the fat of *Picramnia* spp. or *Tariri* (Ber. **27**, R. 20 : C. 1902, I. 1155).

D. DIOLEFINE CARBOXYLIC ACIDS

$\Delta^{\alpha\gamma}$-Diolefinecarboxylic acids are obtained by the two following general methods :

(1) By the condensation of $\alpha\beta$-olefine aldehydes with malonic acid, by means of pyridine (Ber. **35**, 1143).

$$CH_2 : CH{\cdot}CHO + CH_2(COOH)_2 \xrightarrow{C_5H_5N} CH_2 : CH{\cdot}CH : CHCOOH + H_2O + CO_2.$$

(2) By the condensation of olefinealdehydes or ketones by means of halogen fatty acid esters and zinc, and subsequently splitting off water from the β-hydroxyolefine carboxylic esters thus formed, by heating with alkalis (Ber. **35**, 3633 : **36**, 15 : C. 1903, II. 555) :

$$\begin{aligned} CH_3CH : CH{\cdot}CHO + BrZnCH_2CO_2R &\longrightarrow CH_3CH : CH{\cdot}CH(OH)CH_3COOR \\ &\longrightarrow CH_3CH : CH{\cdot}CH : CH{\cdot}COOH. \end{aligned}$$

The lower members of this series polymerize in the warm very easily. When the acids are heated with barium hydroxide, there are formed, not the butadienes corresponding to the acids, but cyclic di- and trimolecular polymers, whose constitution is not quite clear (Ber. **35**, 2119 : **49**, 146).

Butadienecarboxylic acid, $CH_2 : CH{\cdot}CH : CHCO_2H$, m.p. 102°, is formed, together with ethylidene propionic acid (p. 346), by the reduction of *perchlorobutadienecarboxylic acid*, $CCl_2 : CCl{\cdot}CCl : CCl{\cdot}CO_2H$, m.p. 97°, and *perchlorobutinecarboxylic acid*, $CCl_3{\cdot}C : C{\cdot}CCl_2{\cdot}CO_2H$, m.p. 127°. These are products of decomposition resulting from the two hexachloro*cyclo*pentenones (Vol. II) on treatment with alkali (Ber. **28**, 1644).

β-Vinylacrylic acid, $CH_2 : CH{\cdot}CH : CHCOOH$, m.p. 80°, is produced by condensing malonic acid and acrolein in the presence of pyridine, and boiling the resulting product with water. Reduction by sodium amalgam brings about addition at the $\alpha\delta$-carbon atoms (p. 28), forming $\beta\gamma$-pentenoic acid (p. 346). Oxidation with permanganate converts it into racemic acid (Ber. **35**, 1136). The methyl ester forms the product methyl Δ^{γ}-pentene-$\alpha\alpha\epsilon$-tricarboxylate with methyl sodiomalonate, addition of the malonic ester also taking place solely in the $\alpha\delta$-position (J.A.C.S. **48**, 1036 : J.C.S. **1927**, 1060).

Butadienecarboxylic acid (m.p. 102°) and vinylacrylic acid (m.p. 80°) are probably *cis-trans*-isomers.

Sorbic acid, $CH_3CH : CH{\cdot}CH : CH{\cdot}COOH$, m.p. 134·5°, b.p. 228°, is obtained, together with malic acid, from the oil in the unripe juice of the berries of mountain ash (*Sorbus aucuparia*) (1859, *A. W. Hofmann*, Ann. **110**, 129). It exists there in the form of a lactone, the so-called *parasorbic acid* (*q.v.*), which is boiled with sodium hydroxide or hydrochloric acid (Ber. **27**, 351). Synthetically, it is prepared from crotonaldehyde or aldol and malonic acid with pyridine (Ber. **33**, 2140 : Ann. **361**, 89), also from β-hydroxy-$\gamma\delta$-hexenoic acid, by boiling it with a 20% barium hydroxide solution (Ber. **35**, 3636). Oxidation by $KMnO_4$ produces acetaldehyde and racemic acid (*q.v.*), a reaction which reveals the structure of sorbic acid (Ber. **23**, 2377 : **24**, 85) :

$$\underset{\text{Sorbic acid.}}{CH_3CH : CH{\cdot}CH : CH{\cdot}COOH} + H_2O + 4O = CH_3CHO + \underset{\text{Racemic acid.}}{COOH(CHOH)_2COOH}.$$

Sodium amalgam converts it into hydrosorbic acid (p. 347).

Addition of malonic ester to sorbic ester also takes place in the $\alpha\delta$-position, methyl β-methyl-Δ^{γ}-pentene-$\alpha\alpha\epsilon$-tricarboxylate being formed (J.A.C.S. **48**, 1036: J.C.S. **1927**, 1060).

Heated with ammonia, sorbic acid yields a diaminocaproic acid; hydroxylamine brings about a peculiar reaction resulting in acetylacetone dioxime (p. 408) (Ber. **37**, 3316). *Sorbic ethyl ester*, b.p. 95°.

α-Methylsorbic acid, m.p. 91°, **α-ethylsorbic acid**, b.p. 76°, and **$\beta\delta$-dimethylsorbic acid**, m.p. 93°, are obtained by method 2 (above).

$\gamma\epsilon$-Dimethylsorbic acid, b.p. 165°/20 mm., is prepared according to method 1 (p. 353) from α-methyl-β-ethyl acrolein and malonic acid.

Diallylacetic acid, $(CH_2 : CH{\cdot}CH_2)_2CH{\cdot}CO_2H$, b.p. 227°, is obtained from ethyl diallylacetoacetate or diallylmalonic acid. Nitric acid oxidizes it to tricarballylic acid, $(CO_2H{\cdot}CH_2)_2CHCO_2H$.

Geranic acid, $Me_2C : CH[CH_2]_2{\cdot}CMe : CH{\cdot}COOH$, b.p. 153°/11 mm., really belongs to this series, but on account of its importance in terpene chemistry, will be discussed with the terpenes in Vol. II.

Linoleic acid, *Linolic acid*, $C_{18}H_{32}O_2$, $CH_3[CH_2]_2CH : CH[CH_2]_2{\cdot}CH : CH[CH_2]_7COOH$ (?), m.p. − 9°, b.p. 228°/14 mm. (Ber. **58**, 1068), occurs as glyceride in the *drying oils*, which oxidize in the air, becoming covered with a skin and finally solidifying. This oxidation is markedly accelerated by the presence of various compounds such as manganese salts, used as *driers* in the paint and varnish industry. Examples of drying oils are linseed oil, hemp oil, poppy oil and nut oil. The *non-drying oils* such as rape oil contain oleic glycerides.

Linoleic acid forms a *tetrabromide*, m.p. 115°, and by gentle oxidation with permanganate, a tetrahydroxystearic acid, *sativic acid*, m.p. 172° (C. 1909, II. 1984).

Ricinoleic acid can be conveniently treated here, although it is really an unsaturated hydroxy-acid. Ricinoleic acid, $C_{18}H_{34}O_3 = CH_3[CH_2]_5{\cdot}CHOH{\cdot}CH_2{\cdot}CH : CH(CH_2)_7CO_2H$, $[\alpha]_D = +\,6{\cdot}67°$ (Ber. **27**, 3471: Rec. Trav. Chim. **38**, 375) is present in castor oil in the form of a glyceride, $[\alpha]_D = +\,3°$. The lead salt is soluble in ether. Subjected to dry distillation, ricinoleic acid splits into œnanthol, $C_7H_{14}O$, and undecylenic acid, $C_{11}H_{20}O_2$.

Fused with potassium hydroxide, it changes to sebacic acid, $C_8H_{16}(CO_2H)_2$, and *sec.*-octyl alcohol, $C_6H_{13}CHOH{\cdot}CH_3$. It combines with bromine to form a solid *dibromide*. When heated with HI (iodine and phosphorus), it is transformed into iodo-oleic acid, $C_{18}H_{33}IO_2$, which yields stearic acid when heated with zinc and hydrochloric acid (Ber. **29**, 806).

The point of double union between the carbon atoms in ricinoleic acid is ascertained as in the case of oleic acid: (1) by conversion into *ricinostearolic acid*, m.p. 53°, (2) and this into *ketohydroxystearic acid*, m.p. 84°, (3) finally, by the breaking down of the oxime of the latter acid (Ber. **27**, 3121: C. 1900, II. 37).

Nitrous acid converts ricinoleic acid into isomeric *ricinelaidic acid*, m.p. 53° C. (see Ber. **21**, 2735: **27**, R. 629).

The formula for ricinoleic acid derived from the above results is confirmed by ozone oxidation, which yields β-hydroxynonoic acid and azelaic acid (Compt. rend. **150**, 496). With strong sulphuric acid, the sulphuric ester $C_{17}H_{32}(OSO_3H){\cdot}COOH$ is formed (*cf.* C. 1909, II. 1422).

It is remarkable that catalytic hydrogenation of ricinoleic acid leads to the formation of an optically inactive, non-resolvable hydroxystearic acid, although the asymmetric carbon atom should not be affected in this reduction (Walden, Z. angew. Chem. **38**, 811).

Alkyl esters of ricinoleic acid and their *acyl* derivatives, see Ber. **36**, 781.

E. TRIOLEFINECARBOXYLIC ACIDS, $C_nH_{2n-6}O_2$

Elaeostearic acid, $C_{18}H_{30}O_2 = CH_3[CH_2]_2CH : CH{\cdot}CH : CH{\cdot}CH : CH{\cdot}[CH_2]_7COOH$, m.p. 48°, b.p. 235°/12 mm. (Rec. Trav. Chim. **44**, 241: **46**, 619), has been isolated from Japanese wood oil. It can be hydrogenated to stearic acid (Ber. **45**, 2730) and was long regarded as a stereoisomer of linoleic acid. It forms, however, a *tetrabromide*, m.p. 114°, when treated with bromine in chloroform at −15°, which is still unsaturated (Constitution, see Rec. Trav. Chim. **46**, 619).

Linolenic acid, $C_{18}H_{30}O_2 = CH_3{\cdot}CH_2{\cdot}CH : CH{\cdot}CH_2{\cdot}CH : CH{\cdot}CH_2{\cdot}CH : CH[CH_2]_7COOH$, b.p. 157°/0·01 mm., occurs together with linoleic acid in linseed oil and can be separated from this by means of the different solubilities of the zinc salts in alcohol. It forms a *hexabromide*, m.p. 179°. It forms stearic acid on reduction, and propionaldehyde, malonaldehydic acid and azelainaldehydic acid by decomposition of its ozonide, whereby the above formula is derived (Ber. **42**, 1327 : Z. physiol. Chem. **74**, 179).

F. UNSATURATED ACIDS, $C_nH_{2n-8}O_2$

Clupanodonic acid, $C_{18}H_{28}O_2$, occurs as glyceride in fish oils, particularly in Japanese sardine oil. It is an oil with a fish-like odour, and is responsible for the unpleasant odour of fish oils. Reduction yields stearic acid. It forms an *octabromide* (C. 1914, I. 1882).

IV. DIHYDRIC ALCOHOLS OR GLYCOLS AND THEIR OXIDATION PRODUCTS

The glycols are compounds which contain in the molecule two hydroxyl groups, and resemble in many ways the monohydric alcohols which have already been discussed. Like them they yield oxidation products, and both hydroxyl groups may be oxidized to the same degree, yielding dialdehydes, diketones and dicarboxylic acids, or oxidation may affect one hydroxyl group more than the other, such compounds as hydroxyaldehydes, keto-acids, etc., being produced. The number of possible types of oxidation product is, of course, much greater than in the case of the monohydric alcohols, and the derivatives will be discussed in the following order :

1. Glycols, Dihydric Alcohols.
2. Hydroxyaldehydes, Aldehyde Alcohols.
3. Hydroxyketones, Ketone Alcohols.
4. Dialdehydes.
5. Aldehyde Ketones.
6. Diketones.
7. Hydroxyacids, Alcohol Monocarboxylic Acids.
8. Aldehyde Monocarboxylic Acids.
9. Keto-monocarboxylic Acids.
10. Dicarboxylic Acids.

From the very nature of the conditions there are no compounds in any of these series which contain but one carbon atom in the molecule. However, carbonic acid with its exceedingly numerous derivatives will be introduced before the dicarboxylic acids—the carbonic acid group.

Carbonic acid is the simplest dibasic acid ; it is similar, in many respects, to the dicarboxylic acids and a special type for such acids, which, like it, only occur in an anhydride form.

1. DIHYDRIC ALCOHOLS OR GLYCOLS

A. PARAFFIN GLYCOLS

Wurtz (1856) discovered glycol, and thus succeeded in filling the gap between the monohydric alcohols and the triacid alcohol, glycerol. He chose the name glycol to indicate the relation of the new body to alcohol on the one hand and glycerol on the other. Glycols are distinguished as α-, β-, γ-, δ-, etc., according as the hydroxyls are attached to adjacent carbon atoms (1 : 2), or in 1 : 3-, 1 : 4-, and 1 : 5- positions respectively. There are also diprimary, primary-secondary, etc., glycols (consult p. 128). The Geneva names are obtained for the glycols by attaching the final syllable "diol" to the name of the parent hydrocarbon.

Glycols differ from the monohydric alcohols just as the hydroxides of bivalent metals differ from those of univalent metals, or as a dibasic acid from a monobasic acid. As a rule, the reactions leading from the monohydric alcohols and glycols to their corresponding derivatives are very similar. In the case of the glycols, a series of mono-substitution products can be obtained, which still show the characters of a monohydric alcohol. Ethylene glycol, for example, is capable of forming a mono- and dialkali glycolate, mono- and dialkyl ethers, mono- and di- esters, *e.g.*:

$\begin{array}{l} CH_2{\cdot}OH \\ \vert \\ CH_2{\cdot}OH \end{array}$ Glycol.	$\begin{array}{l} CH_2{\cdot}ONa \\ \vert \\ CH_2{\cdot}OH \end{array}$ Monosodium glycolate.	$\begin{array}{l} CH_2{\cdot}O{\cdot}C_2H_5 \\ \vert \\ CH_2{\cdot}OH \end{array}$ Glycol mono-ethyl ether.	$\begin{array}{l} CH_2{\cdot}O{\cdot}COCH_3 \\ \vert \\ CH_2{\cdot}OH \end{array}$ Glycol monacetate.
	$\begin{array}{l} CH_2{\cdot}ONa \\ \vert \\ CH_2{\cdot}ONa \end{array}$ Disodium glycolate.	$\begin{array}{l} CH_2{\cdot}O{\cdot}C_2H_5 \\ \vert \\ CH_2{\cdot}O{\cdot}C_2H_5 \end{array}$ Glycol diethyl ether.	$\begin{array}{l} CH_2{\cdot}O{\cdot}COCH_3 \\ \vert \\ CH_2{\cdot}O{\cdot}COCH_3 \end{array}$ Glycol diacetate.

All the mono compounds also exhibit the character of monohydric alcohols; they and the di- compounds, which have been mentioned, can be obtained from the glycols by the same methods as the corresponding products of the monohydric alcohols.

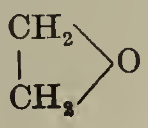
The sulphur- and nitrogen-containing derivatives of the glycols correspond with like derivatives of the monohydric alcohols:

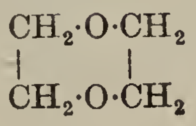
$\begin{array}{l} CH_2{\cdot}SH \\ \vert \\ CH_2{\cdot}OH \end{array}$ Monothio-glycol.	$\begin{array}{l} CH_2{\cdot}SH \\ \vert \\ CH_2{\cdot}SH \end{array}$ Dithio-glycol.	$\begin{array}{l} CH_2{\cdot}NH_2 \\ \vert \\ CH_2{\cdot}OH \end{array}$ Hydroxyethylamine.	$\begin{array}{l} CH_2{\cdot}NH_2 \\ \vert \\ CH_2{\cdot}NH_2 \end{array}$ Ethylene diamine.

The aldehydes have been repeatedly spoken of as the anhydrides of dihydric alcohols, in which the two hydroxyl groups are joined to the same carbon atom, and which can only exist under special conditions. Yet, the ethers (or acetals), esters and other derivatives of these hypothetical compounds are stable. These bodies are naturally isomeric with the corresponding derivatives of the dihydric alcohols, in which the hydroxyl groups are attached to different carbon atoms. The following, for example, are isomeric:

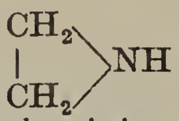
$CH_3{\cdot}CH{<}\begin{array}{l} O{\cdot}C_2H_5 \\ O{\cdot}C_2H_5 \end{array}$	Acetal	and	$\begin{array}{l} CH_2{\cdot}O{\cdot}C_2H_5 \\ \cdot \\ CH_2{\cdot}O{\cdot}C_2H_5 \end{array}$	Glycol diethyl ether
$CH_3{\cdot}CH{<}\begin{array}{l} O{\cdot}COCH_3 \\ O{\cdot}COCH_3 \end{array}$	Ethylidene diacetate	and	$\begin{array}{l} CH_2{\cdot}O{\cdot}COCH_3 \\ \cdot \\ CH_2{\cdot}O{\cdot}COCH_3 \end{array}$	Glycol diacetate
$CH_3{\cdot}CH{<}\begin{array}{l} OH \\ NH_2 \end{array}$	Aldehyde ammonia	and	$\begin{array}{l} CH_2OH \\ \cdot \\ CH_2NH_2 \end{array}$	Hydroxyethylamine.

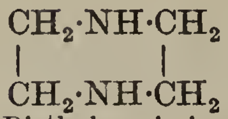
The *cyclic derivatives of the glycols* are extremely characteristic. Thus, glycol yields two cyclic ethers:

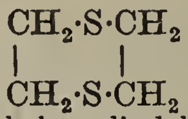

Ethylene oxide.

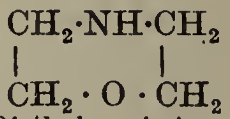

Diethylene oxide.

and also sulphur- and nitrogen-compounds corresponding with diethylene oxide:


Ethylene imine.


$$\begin{array}{l}CH_2{\cdot}NH{\cdot}CH_2\\ |\qquad\quad\ |\\ CH_2{\cdot}NH{\cdot}CH_2\end{array}$$
Diethylene imine.

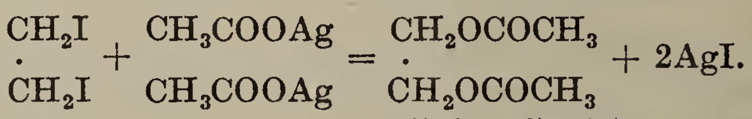

$$\begin{array}{l}CH_2{\cdot}S{\cdot}CH_2\\ |\qquad |\\ CH_2{\cdot}S{\cdot}CH_2\end{array}$$
Diethylene disulphide.


$$\begin{array}{l}CH_2{\cdot}NH{\cdot}CH_2\\ |\qquad\quad\ |\\ CH_2 \cdot O \cdot CH_2\end{array}$$
Diethylene imine oxide.

Methods of Formation.—The first three methods are concerned with the olefines, and lead, according to the constitution of the latter, to glycols of every description.

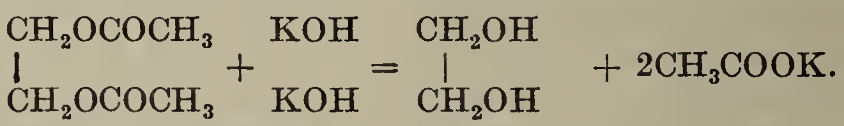
(1) The halogen addition products of the olefines—the alkylene halides—may be regarded as the halogen acid esters of the glycols. When these are acted on by alkalis, with the purpose of exchanging hydroxyl for their halogen, by loss of halogen acid, they pass first into monohalogen olefines and then into acetylenes. Wurtz observed that it was only necessary to treat the alkylene halides with acetates in order to reach the acetic esters of the glycols, and then, by saponification with alkalis, to obtain the glycols.

The alkylene halides are heated (p. 370) with silver acetate and glacial acetic acid, or with potassium acetate in alcoholic solution:

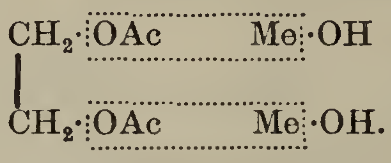

$$\begin{array}{l}CH_2I\\ \cdot\\ CH_2I\end{array} + \begin{array}{l}CH_3COOAg\\ \\ CH_3COOAg\end{array} = \begin{array}{l}CH_2OCOCH_3\\ \cdot\\ CH_2OCOCH_3\end{array} + 2AgI.$$
Ethylene diacetate.

Inasmuch as the olefines are prepared from monohydric alcohols by withdrawal of water, and are transformed by the addition of halogens into alkylene halides, the preceding reaction may be regarded as a method of converting monohydric alcohols into dihydric alcohols or glycols.

The resulting acetic esters are purified by distillation, and then saponified by KOH or barium hydroxide solution (C. 1899, I. 968):

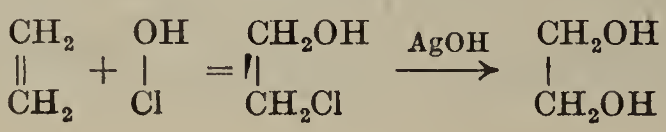

$$\begin{array}{l}CH_2OCOCH_3\\ |\\ CH_2OCOCH_3\end{array} + \begin{array}{l}KOH\\ \\ KOH\end{array} = \begin{array}{l}CH_2OH\\ |\\ CH_2OH\end{array} + 2CH_3COOK.$$

A more useful method than hydrolysis with aqueous alkali is that of hydrolysis with methyl alcoholic hydrochloric acid, which takes place in a homogeneous system and from which the resulting products can easily be separated:

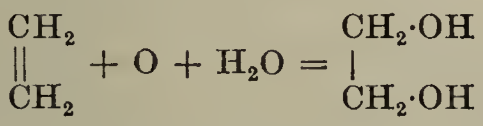

$$\begin{array}{l}CH_2{\cdot}\vdots OAc \qquad Me\vdots{\cdot}OH\\ |\\ CH_2{\cdot}\vdots OAc \qquad Me\vdots{\cdot}OH.\end{array}$$

A direct conversion of alkylene halides into glycols may be attained by heating them with water (Ann. **186**, 293), with water and lead oxide, or sodium and potassium carbonates.

(2) Another procedure consists in shaking the alkylenes, C_nH_{2n}, with aqueous hypochlorous acid, and afterwards decomposing the chlorhydrins formed with moist silver oxide:

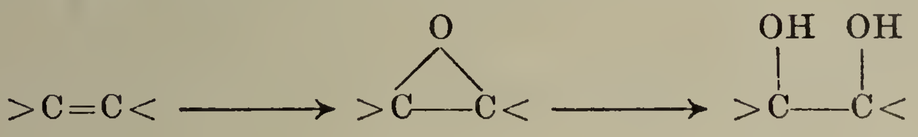

$$\begin{array}{l}CH_2\\ \|\\ CH_2\end{array} + \begin{array}{l}OH\\ |\\ Cl\end{array} = \begin{array}{l}CH_2OH\\ |\\ CH_2Cl\end{array} \xrightarrow{AgOH} \begin{array}{l}CH_2OH\\ |\\ CH_2OH\end{array}$$

(3) By the *oxidation of the olefines* (*a*) in alkaline solution (p. 103) (Wagner, Ber. **21**, 1230) with potassium permanganate, or (*b*) with hydrogen peroxide. Thus, ethylene yields ethylene glycol; *iso*butylene, iso*butylene glycol*, $(CH_3)_2{\cdot}C(OH){\cdot}CH_2{\cdot}OH$:

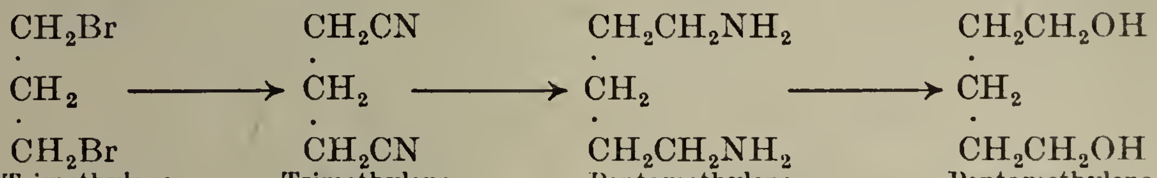


$$\begin{matrix}CH_2\\ \|\\ CH_2\end{matrix} + O + H_2O = \begin{matrix}CH_2{\cdot}OH\\ |\\ CH_2{\cdot}OH\end{matrix}$$

The preparation of αβ-glycols from olefines can be carried out smoothly by the use of perbenzoic acid in an indifferent solvent. The first-formed ethylene oxide is hydrolysed by water to the glycol (*Prileschajew*, Ber. **42**, 4811: **43**, 959):



(4) By the action of nitrous acid on diamines (p. 382). As these can be obtained from the corresponding nitriles of dibasic acids, and the nitriles themselves from alkylene halides, these reactions not only ally the classes of derivatives mentioned, but they afford a means of building up the glycols:



$$\begin{matrix}CH_2Br\\ \cdot\\ CH_2\\ \cdot\\ CH_2Br\end{matrix} \longrightarrow \begin{matrix}CH_2CN\\ \cdot\\ CH_2\\ \cdot\\ CH_2CN\end{matrix} \longrightarrow \begin{matrix}CH_2CH_2NH_2\\ \cdot\\ CH_2\\ \cdot\\ CH_2CH_2NH_2\end{matrix} \longrightarrow \begin{matrix}CH_2CH_2OH\\ \cdot\\ CH_2\\ \cdot\\ CH_2CH_2OH\end{matrix}$$

Trimethylene bromide. Trimethylene cyanide. Pentamethylene diamine. Pentamethylene glycol.

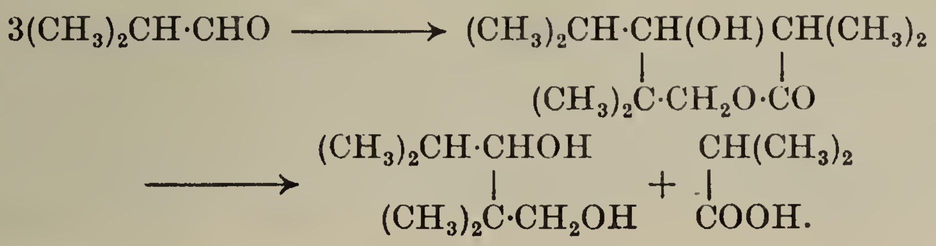
Besides the normal glycols, isomeric glycols are sometimes obtained, as well as olefine alcohols and diolefines (Ber. **40**, 2589).

(5) By the catalytic reduction of acetylenic and diacetylenic glycols (p. 366) with hydrogen and finely-divided platinum (Compt. rend. **150**, 1761: **156**, 1623).

(6) By reduction of (*a*) *aldehydes* or *keto-alcohols, dialdehydes* or *diketones*.

By this means the α-keto-alcohols butyroin and caproin (p. 394) yield the stereoisomeric forms of δε-octane-diol and ζη-dodecane-diol; aldol (p. 390) gives αγ-butylene glycol; acetobutyl alcohol (p. 395) gives αε-hexane-diol, and acetonylacetone (p. 404) yields βε-hexane-diol.

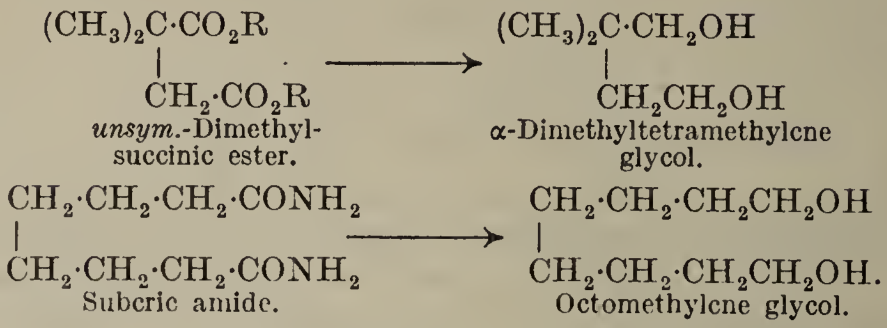
Akin to these reactions is the formation of glycol by the condensation of *iso*butyraldehyde, alone or when mixed with other aldehydes, by means of alcoholic potassium hydroxide. An aldol (p. 390) is first formed, of which the aldehydic group is acted on by excess of aldehyde producing a monobutyrin of the αγ-glycol (comp. p. 230), which in turn is decomposed by hydrolysis into the glycol and *iso*butyric acid (Monatsh. **17**, 68: **19**, 16):



$$3(CH_3)_2CH{\cdot}CHO \longrightarrow \begin{matrix}(CH_3)_2CH{\cdot}CH(OH)\,CH(CH_3)_2\\ |\qquad\qquad |\\ (CH_3)_2C{\cdot}CH_2O{\cdot}CO\end{matrix}$$

$$\longrightarrow \begin{matrix}(CH_3)_2CH{\cdot}CHOH\\ |\\ (CH_3)_2C{\cdot}CH_2OH\end{matrix} + \begin{matrix}CH(CH_3)_2\\ |\\ COOH.\end{matrix}$$

By the reduction of (*b*) *dicarboxylic esters or amides* by sodium and alcohol (C. 1905, II. 1701).



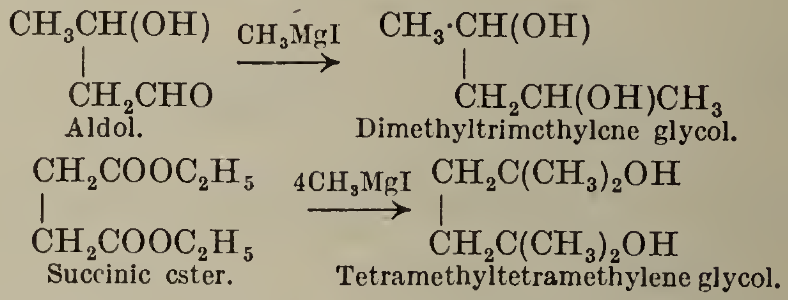
$$\begin{array}{l}(CH_3)_2C\cdot CO_2R\\ \quad|\\ \quad CH_2\cdot CO_2R\\ \textit{unsym.}\text{-Dimethyl-}\\ \text{succinic ester.}\end{array} \longrightarrow \begin{array}{l}(CH_3)_2C\cdot CH_2OH\\ \quad|\\ \quad CH_2CH_2OH\\ \alpha\text{-Dimethyltetramethylene}\\ \text{glycol.}\end{array}$$

$$\begin{array}{l}CH_2\cdot CH_2\cdot CH_2\cdot CONH_2\\ |\\ CH_2\cdot CH_2\cdot CH_2\cdot CONH_2\\ \text{Suberic amide.}\end{array} \longrightarrow \begin{array}{l}CH_2\cdot CH_2\cdot CH_2CH_2OH\\ |\\ CH_2\cdot CH_2\cdot CH_2CH_2OH.\\ \text{Octomethylene glycol.}\end{array}$$

Lactones, the cyclic esters of γ-, δ-, or ε-hydroxy-carboxylic esters, are also reduced to glycols by sodium and alcohol (Ber. **39,** 2851); similarly, β-ethoxyl propionic ester yields the ethyl ether of trimethylene glycol (C. 1905, I. 25).

Nucleus Synthetic Methods

(7) Aldehyde alcohols, diketones, keto-carboxylic esters, dicarboxylic esters, all react with alkyl magnesium halides (p. 219) forming glycols, accompanied by the entry of an alkyl group (Ber. **35,** 2138: **42,** 2500: Monatsh. **28,** 997: Ann. **396,** 250: C. 1904, I. 578: 1906, II. 1639: 1907, I. 627):



$$\begin{array}{l}CH_3CH(OH)\\ \quad|\\ \quad CH_2CHO\\ \quad\text{Aldol.}\end{array} \xrightarrow{CH_3MgI} \begin{array}{l}CH_3\cdot CH(OH)\\ \quad|\\ \quad CH_2CH(OH)CH_3\\ \text{Dimethyltrimethylene glycol.}\end{array}$$

$$\begin{array}{l}CH_2COOC_2H_5\\ |\\ CH_2COOC_2H_5\\ \text{Succinic ester.}\end{array} \xrightarrow{4CH_3MgI} \begin{array}{l}CH_2C(CH_3)_2OH\\ |\\ CH_2C(CH_3)_2OH\\ \text{Tetramethyltetramethylene glycol.}\end{array}$$

By the same reagent alkoxy-ketones and alkoxy-carboxylic esters are converted into monoalkyl ethers of the glycols (C. 1904, I. 504). Similarly, lactones yield primary-tertiary glycols (C. 1907, I. 708).

Monoalkyl derivatives of the glycols are also obtained by the action of chloromethyl alkyl ethers on ketones in the presence of magnesium or other metals (C. 1907, I. 681).

(8) The action of metals, such as sodium or magnesium, on many halogen-hydrin compounds of the ethers, either alone or mixed with halogen methyl alkyl ethers (p. 243), is to build up the ethers of the higher glycols from lower members (C. 1903, I. 455: 1904, I. 1401):

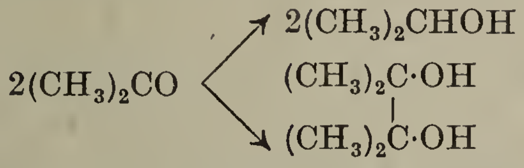
$$\underset{\gamma\text{-Phenoxypropyl iodide.}}{2C_6H_5O\cdot CH_2CH_2CH_2I} \xrightarrow{Na} C_6H_5O[CH_2]_6OC_6H_5 \longrightarrow \underset{\text{Hexamethylene glycol.}}{HO[CH_2]_6OH}$$

$$\underset{\substack{\text{Amyloxypropyl}\\ \text{bromide.}}}{C_5H_{11}O[CH_2]_3Br} + BrCH_2OC_5H_{11} \xrightarrow{Mg} C_5H_{11}O[CH_2]_4OC_5H_{11} \longrightarrow \underset{\substack{\text{Tetramethylene}\\ \text{glycol.}}}{HO[CH_2]_4OH}$$

The dimethyl ethers of diprimary glycols are obtained by the action of chloromethyl ether on the dimagnesium compounds of the higher alkylene dihalides (Bull. Soc. Chim. [4] **7,** 327: Ber. **45,** 1973).

(9) The ditertiary glycols or pinacols are obtained, along with secondary alcohols, by the reduction of ketones. The simplest pina-

cone, tetramethylethylene glycol, is thus obtained from acetone (Friedel):



$$2(CH_3)_2CO \rightarrow 2(CH_3)_2CHOH \quad ; \quad 2(CH_3)_2CO \rightarrow \begin{array}{l}(CH_3)_2C{\cdot}OH\\ \quad\;\;|\\ (CH_3)_2C{\cdot}OH\end{array}$$

The formation of pinacones takes place particularly readily when ketones are warmed with magnesium- or aluminium-amalgam in absence of water. The corresponding metallic derivative of the pinacone is thus formed and can be decomposed with liberation of the pinacone, either by water or by dilute acids (Bull. Soc. Chim. [4] **7,** 459: D.R.P. 241896, C. 1912, I. 176: D.R.P. 251330/1, C. 1912, II. 1318).

Di-secondary glycols are formed in small quantity by the action of magnesium amalgam on aldehydes, and by the electrolytic reduction of aldehydes in acid solution (Atti. R. Accad. Lincei. [5] **22,** II. 681: D.R.P. 277392, C. 1914, II. 674):

$$2CH_3CHO \longrightarrow CH_3{\cdot}CH(OH){\cdot}CH(OH){\cdot}CH_3$$

(10) The diakyl ethers of some glycols are obtained by the electrolysis of the alkoxycarboxylic acids, similarly to the formation of ethane from potassium acetate (see p. 94: C. 1905, I. 1698).

(11) The formation of glycols by the condensation of ketones and alcohols under the influence of light, and of their ethers from alkyl ethers and ketones is noteworthy (Ber. **43,** 945: **44,** 1280, 1554):

$$(CH_3)_2CO + CH_3CH_2OH \longrightarrow (CH_3)_2C(OH){\cdot}CH(OH){\cdot}CH_3.$$

Properties.—The glycols are neutral, thick liquids, holding, as far as their properties are concerned, a place intermediate between the monohydric alcohols and trihydric glycerol. The solubility of a compound in water increases according to the accumulation of OH groups in it, and becomes correspondingly less soluble in alcohol, and especially in ether. There is an appreciable rise in the boiling point, whilst the body acquires at the same time a sweet taste. In accord with this, the glycols have a sweetish taste, are very easily soluble in water, slightly soluble in ether, and boil much higher (about 100°) than the corresponding monohydric alcohols. As the number and dimensions of the alkyl groups grow, the higher homologues become increasingly soluble in ether, and the taste becomes sharper and, in some cases, burning.

The reactions of the glycols with dehydrating agents are important, and the products depend upon the relative positions of the hydroxyl groups.

(i) The 1 : 2 glycols yield aldehydes and ketones:

$$(CH_3)_2C(OH){\cdot}CH_2OH \longrightarrow (CH_3)_2CH{\cdot}CHO$$

$$(C_6H_5)(C_3H_5)C(OH){\cdot}CH(OH){\cdot}C_6H_5 \longrightarrow (C_6H_5)_2(C_3H_5)C{\cdot}CHO$$

(C. 1923, III. 1017)

$$CH_3{\cdot}CH(OH){\cdot}CH(OH){\cdot}CH_3 \longrightarrow CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_3.$$

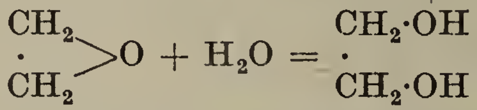
For the behaviour of ditertiary glycols under these conditions, see Pinacone, p. 363.

(ii) 1 : 3-glycols form cyclic oxides and also aldehydes and ketones (Monatsh. **23,** 60):

(iii) 1 : 4- and 1 : 5-glycols yield cyclic oxides. The higher glycols, 1 : 6-, 1 : 8-, 1 : 9-, 1 : 10-, form 1 : 5-oxides, with narrowing of the oxide ring, under the influence of concentrated sulphuric acid (Monatsh. **43**, 589) (see p. 368).

Ethylene glycol, *Glycol,* [1, 2-Ethanediol], $CH_2OH{\cdot}CH_2OH$, m.p. − 11·5°, b.p. 197·5°, $D_0 = 1{\cdot}125$, is miscible with water and alcohol. Ether dissolves but small quantities of it.

It may be obtained from ethylene through ethylene bromide, ethylene chlorhydrin (general method of formation, p. 358) or by direct oxidation; and also from ethylene oxide by the absorption of water:



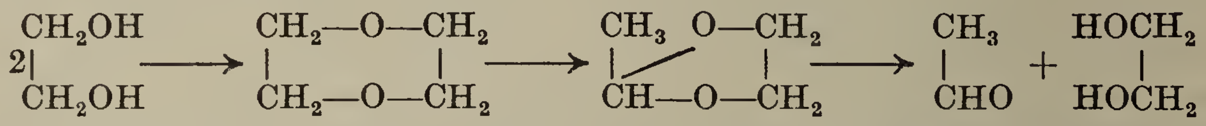
$$\begin{matrix}CH_2\\ \cdot\\ CH_2\end{matrix}{>}O + H_2O = \begin{matrix}CH_2{\cdot}OH\\ \cdot\\ CH_2{\cdot}OH\end{matrix}$$

Preparation.—A mixture of ethylene bromide, potassium carbonate and water is boiled under a reflex condenser, until all the bromide is dissolved (Ann. **192**, 240, 250). Or the ethylene bromide may be converted by heating with anhydrous potassium acetate into glycol diacetate, which yields glycol when hydrolysed with alkali hydroxide (Ber. **29**, R. 287; C. 1899, I. 968).

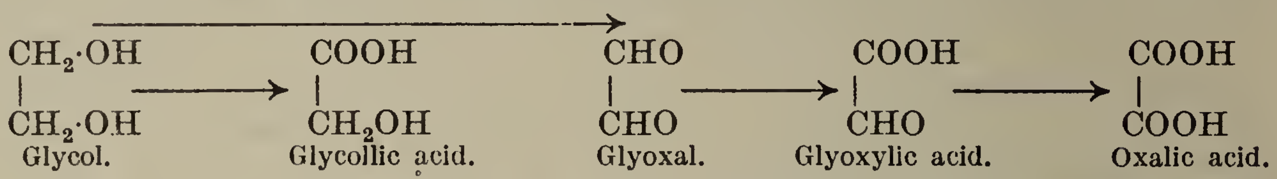
Glycol can be directly obtained from ethylene bromide by heating it with 3 mols. of sodium formate in the presence of methyl alcohol in the autoclave at 170°. The first-formed glycol diformate is alcoholysed by the methyl alcohol.

Reactions.—(1) *Dehydration.* On heating ethylene glycol with zinc chloride to 250° water is eliminated and acetaldehyde and crotonaldehyde are formed; at 210° with water, only acetaldehyde results.

When ethylene glycol is distilled with 4% concentrated sulphuric acid, not only acetaldehyde and ethylidene ethylene ether (p. 367) are formed, but also diethylene oxide. Further treatment of this oxide with sulphuric acid or zinc chloride results in the production of acetaldehyde (C. 1907, I. 15):



(2) *Oxidation.* Nitric acid oxidizes glycol to glycollic acid and glyoxal, glyoxylic acid and oxalic acid. The first oxidation product, glycol aldehyde (*q.v.*), is further oxidized too rapidly to be identified:



$$\begin{matrix}CH_2{\cdot}OH\\ |\\ CH_2{\cdot}OH\end{matrix} \longrightarrow \begin{matrix}COOH\\ |\\ CH_2OH\end{matrix} \qquad \begin{matrix}CHO\\ |\\ CHO\end{matrix} \longrightarrow \begin{matrix}COOH\\ |\\ CHO\end{matrix} \longrightarrow \begin{matrix}COOH\\ |\\ COOH\end{matrix}$$

(3) When glycol is heated with potassium hydroxide to 250°, it is oxidized to oxalic acid with evolution of hydrogen.

(4) Heated to 160° with concentrated hydrochloric acid, glycol chlorhydrin results, which at 200° is converted into ethylene dichloride.

(5) Ethylene dichloride is also produced when PCl_5 acts on glycol.

(6) A mixture of nitric and sulphuric acids changes glycol into glycol dinitrate.

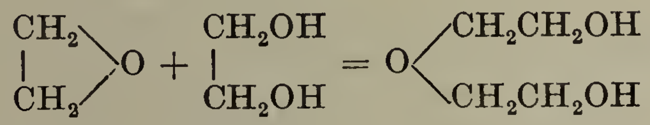
(7) Concentrated sulphuric acid and glycol yield glycol sulphate.

(8) The acid chlorides or acid anhydrides produce mono- and diesters of glycol.

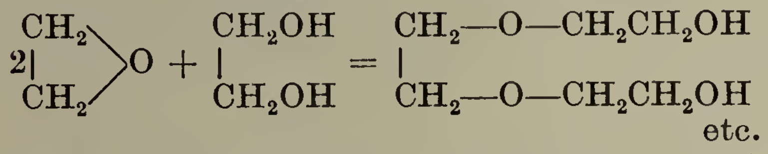
(9) Metallic sodium dissolves in glycol, forming sodium glycolate, $C_2H_4{<}\genfrac{}{}{0pt}{}{OH}{ONa}$, and (at 170°) disodium glycolate, $C_2H_4(ONa)_2$. Both

are white, crystalline substances, regenerating glycol with water. The alkyl halides convert them into the corresponding ethers.

Polyethylene Glycols.—Ethylene oxide absorbs water to form glycol. The latter and ethylene oxide unite at 100° in varying proportions, thus yielding the polyethylene glycols:



Diethylene glycol, b.p. 250°.



Triethylene glycol, b.p. 287°.

The polyglycols are thick liquids, with high boiling points. They behave like the glycols. Ether-acids may be obtained from them by oxidation with dilute nitric acid; thus diglycollic acid (*q.v.*) is formed from diethylene alcohol.

There are two series of homologues of ethylene glycol; the one resulting from alkyl substitution, and the other, including the 1 : 3-, 1 : 4-, 1 : 5-glycols, etc., produced by the insertion of an alkyl group between the carbinol groups.

Homologous 1 : 2-Glycols

α-Propylene glycol, [Propanediol-1 : 2], $CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$, b.p. 188°, $D_0 = 1{\cdot}015$, is obtained from propylene bromide or chloride. It is most readily prepared by distilling glycerol with sodium hydroxide (Ber. **13**, 1805). Platinum black oxidizes it to lactic acid. Only acetic acid is formed when chromic acid is the oxidizing agent. Concentrated hydriodic acid changes it to *iso*propyl alcohol and its iodide. Heated with water at about 190° it yields propylaldehyde and acetone. It contains an asymmetric carbon atom, and when exposed to the action of *Bacterium termo*, becomes optically active (Ber. **14**, 843).

The following glycols can be obtained from their dibromides:

α-Butylene glycol, *Ethylethylene glycol*, $C_2H_5CH(OH){\cdot}CH_2OH$, b.p. 192°.

βγ-Butylene glycol, sym.-*Dimethylethylene glycol*, $CH_3CH(OH){\cdot}CH(OH){\cdot}CH_3$, b.p. 184°.

***iso*Butylene glycol,** unsym.-*Dimethylethylene glycol*, $(CH_3)_2C(OH){\cdot}CH_2(OH)$, b.p. 177°.

α-*iso*Amylene glycol, iso*Propylethylene glycol*, $(CH_3)_2CH{\cdot}CH(OH){\cdot}CH_2OH$, b.p. 206°.

β-*iso*Amylene glycol, *Trimethylethylene glycol*, $(CH_3)_2C(OH){\cdot}CH(OH)CH_3$, b.p. 177°.

β-Amylene glycol, sym.-*Methylethylethylene glycol*, $C_2H_5CH(OH)CH(OH){\cdot}CH_3$, b.p. 187°.

sym.-**Dipropylethylene glycol,** *δε-Octanediol*, $C_3H_7CH(OH){\cdot}CH(OH)C_3H_7$, occurs in two modifications; α-form, liquid, b.p. 115–120°/10 mm., β-form, m.p. 125°, and is prepared by reduction of butyroin (p. 394) by sodium and alcohol.

sym.-**Diamylethylene glycol,** *ζη-Dodecanediol*, α-form, m.p. 54°, b.p. 155–160°/10 mm.; β-form, m.p. 136°, is produced when capronoin is reduced by sodium and alcohol (C. 1906, II. 1114).

Pinacone, *Pinacol, Tetramethylethylene glycol*, $(CH_3)_2{\cdot}C(OH){\cdot}C(OH){\cdot}(CH_3)_2 + 6H_2O$, m.p. 42°, *anhydrous*, m.p. 38°, b.p. 171–172°, is formed, together with *iso*propyl alcohol, from acetone by the action of sodium or magnesium and mercuric chloride (C. 1906, II. 148) or by electrolysis (Ber. **27**, 454: C. 1900, II. 794) (see method of formation, No. 9, p. 361). Further, by the action of $IMgCH_3$ on diacetyl or oxalic ester (mode of formation, No. 7*a*). It crystallizes from its aqueous solution in quadratic plates (hence the name, from *πίναξ*, plate), and gradually effloresces on exposure.

In common with other pinacols (p. 360), dilute sulphuric or hydrochloric acids cause it to lose water and undergo intramolecular change, forming *pinacolin* or methyl *tert.*-butyl ketone (p. 265). An isomer of this substance, tetramethylethylene oxide (p. 368), very readily absorbs water forming pinacone.

Similarly to pinacone, a whole series of tetraalkylethylene glycols can be prepared by reduction of aliphatic ketones, known collectively as pinacones, which behave towards dilute sulphuric and hydrochloric acids as pinacone itself does. Comp. methyl *iso*propyl pinacone, C. 1903, II. 23.

1 : 3-Glycols

Trimethylene glycol [Propanediol-1, 3], $CH_2OH{\cdot}CH_2CH_2OH$, b.p. 216°, $D{\cdot}_0 = 1{\cdot}065$, is obtained from trimethylene bromide (Ber. **16**, 393); or by the fermentation of glycerol by Schizomycetes, together with *n*-butyl alcohol (Ber. **20**, R. 706). It is isomeric with α-propylene glycol. Moderate oxidizing agents produce β-hydroxypropionic acid (hydracrylic acid); sulphuric acid changes it into propionaldehyde and acetone (C. 1904, I. 1401).

β-**Butylene glycol,** *β-Methyltrimethylene glycol* [Butanediol-1, 3], $CH_3CH(OH)\text{-}CH_2OH$, b.p. 207°, is obtained by the reduction of aldol (p. 390); 50% sulphuric acid converts it into butyraldehyde and methyl ethyl ketone (comp. p. 361, and C. 1904, I. 1400).

*γ-iso***Amylene glycol,** *αα-Dimethyltrimethylene glycol,* $(CH_3)_2C(OH){\cdot}CH_2CH_2\text{-}OH$, b.p. 203°, is obtained from the bromide (Ber. **29**, R. 92).

sym.-**Dimethyltrimethylene glycol,** *βδ-Pentanediol,* $CH_3CH(OH)CH_2CH\text{-}(OH)CH_3$, b.p. 199°, is prepared by reduction of hydracetylacetone (p. 394); and by the action of magnesium methyl iodide on aldol (C. 1904, I. 1327; Ber. **37**, 4730).

ααγ-**Trimethyltrimethylene glycol,** *β-Methyl-βε-pentanediol,* $(CH_3)_2C(OH)\text{-}CH_2CH_2CH(OH)CH_3$, b.p. 194°, is obtained by reduction of diacetone alcohol (p. 395).

sym.-**Tetramethyltrimethylene glycol,** *βε-Dimethyl-βε-pentanediol,* $(CH_3)_2\text{-}C(OH){\cdot}CH_2{\cdot}C(OH)(CH_3)_2$, b.p. 98°/13 mm., results from the action of CH_3MgI on diacetone alcohol (C. 1902, I. 455: Ber. **37**, 4731).

Hexamethyltrimethylene glycol (*βγγδ-tetramethylpentane-βδ-diol*), $Me_2C\text{-}(OH){\cdot}CMe_2{\cdot}CMe_2OH$, m.p. 76°, b.p. 234°, is formed from dimethylmalonic ester and magnesium methyl iodide: it breaks down on heating with acids into acetone and tetramethylethylene (C. 1914, II. 1261).

A series of higher homologues of the 1 : 3-glycols is obtained from the condensation of *iso*butyraldehyde with other aldehydes, or the *iso*butyl aldols, by means of alcoholic potassium hydroxide (method of formation No. 6*a*, p. 359).

ββ-**Dimethyltrimethylene glycol,** *Pentaglycol,* $(CH_3)_2C(CH_2OH)_2$, m.p. 129°, b.p. 206°. Heated with H_2SO_4 it forms *iso*valeric aldehyde, *iso*propyl methyl ketone and a cyclic oxide (C. 1900, II. 36).

αββ-**Trimethyltrimethylene glycol,** $CH_2(OH)C(CH_3)_2CH(OH)CH_3$, b.p. 207°, and *αββ*-**Dimethylethyltrimethylene glycol,** m.p. 81°, are obtained from *iso*butyraldehyde, and acetaldehyde and propionaldehyde, respectively. *αββ*-**Dimethyl*iso*propyltrimethylene glycol,** $CH_2(OH)C(CH_3)_2CH(OH)C_3H_7$, m.p. 51°, b.p. 223°, is prepared from *iso*butyl aldehyde alone. This substance on oxidation yields first a hydroxy-acid and then di*iso*propyl ketone.

sym.-**Tetramethyl-*β*-ethyltrimethylene glycol,** $(CH_3)_2C(OH)CH(C_2H_5)C\text{-}(OH)(CH_3)_2$, b.p. 128°/11 mm., is obtained from ethylacetoacetic ester and CH_3MgI (mode of formation 7, p. 360) (C. 1902, I. 1197).

1 : 4-Glycols

Tetramethylene glycol, [Butanediol-1 : 4], $HO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2CH_2OH$, b.p. 202–203°, $D = 1{\cdot}011$, is prepared from tetramethylenedinitramine and sulphuric acid (Ber. **23**, R. 506); also, by reduction of succindialdehyde (p. 399), by aluminium amalgam. It possesses an unpleasant odour of leeks (Ber. **35**, 1187). The *diamyl ether* results from the electrolysis of the potassium salt of β-amyloxypropionic acid (C. 1901, I. 613: 1905, I. 1698).

α-**Methyltetramethylene glycol,** (*αδ-Pentanediol*), $CH_3{\cdot}CH(OH)CH_2CH_2\text{-}CH_2OH$, b.p. 123–126°/16 mm., with partial decomposition into γ-pentylene oxide and water on heating. It is obtained from acetopropyl alcohol (C. 1903, II. 531) and from γ-valerolactone by reduction (Ber. **39**, 2851).

β-**Methyltetramethylene glycol,** $CH_2OH{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2OH$, b.p. 124°/13 mm., is obtained by the reduction of pyrotartaric acid with sodium and alcohol (Ann. **383**, 167).

αα-Dimethyltetramethylene glycol, *β-Methyl-βε-pentanediol,* $(CH_3)_2C(OH)CH_2CH_2CH_2OH$, b.p. 222°, results from the action of CH_3MgI on butyrolactone or acetopropyl alcohol (C. 1907, I. 708 : Monatsh. **28**, 1006).

ββ-Dimethyltetramethylene glycol, $CH_2(OH)C(CH_3)_2CH_2CH_2OH$, b.p. 123°/10 mm., is produced from *unsym.*-dimethylsuccinic ester by reduction with sodium and alcohol (C. 1905, II. 178).

βε-Hexylene glycol, *βε-Hexanediol,* $CH_3CH(OH)CH_2CH_2CH(OH)CH_3$, b.p. 217°, is easily obtained by the reduction of acetonyl acetone by sodium amalgam (Ber. **35**, 1335).

βε-Dimethylhexane-βε-diol, $Me_2C(OH){\cdot}CH_2{\cdot}CH_2{\cdot}CMe_2OH$, m.p. (anhyd.) 91°, + $6H_2O$, 41°, is obtained from lævulinic ester or succinic ester and magnesium methyl iodide (C. 1906, II. 1639 : 1909, II. 797).

1 : 5-Glycols

Pentamethylene glycol, *αε-Pentanediol,* $HOCH_2{\cdot}CH_2{\cdot}CH_2CH_2CH_2OH$, b.p. 239°, $D_{18} = 0{\cdot}994$, is obtained from pentamethylene diamine (mode of formation 4, p. 359) (Ber. **40**, 2559). The *diamyl ether* is prepared from δ-amyloxybutyl bromide, magnesium and bromomethyl amyl ether (mode of formation 8, p. 360) (C. 1904, II. 587).

αε-Hexanediol, $CH_3CH(OH)[CH_2]_3CH_2OH$, b.p. 235°/710 mm., is produced from acetobutyl alcohol (p. 395).

1 : 6-, 1 : 7-, 1 : 8-Glycols, etc.

The melting points of these polymethylene glycols appear to follow the same rule as those of the normal paraffin mono- and di-carboxylic acids and other homologous series (p. 58), namely, that those of members possessing an odd number of atoms lie lower than those of the neighbouring even-numbered members (C. 1904, II. 1698).

Hexamethylene glycol, *αζ-Hexanediol,* $HO[CH_2]_6OH$, m.p. 42°, b.p. 250°, is prepared from hexamethylene dibromide or diacetate ; and from adipic ester by reduction. Its *dialkyl ethers* are obtained from γ-alkoxypropyl halides by the action of sodium (methods of formation 6*b* and 8 (p. 360) ; and from γ-amyloxybutyric acid by electrolysis (Ber. **27**, R. 735 : C. 1905, I. 1698 : II. 1701).

Heptamethylene glycol, *diethyl ether,* $C_2H_5O{\cdot}[CH_2]_7OC_2H_5$, b.p. 225°, results from the interaction of η-ethoxyhexyl iodide, magnesium and iodomethyl ethyl ether (mode of formation 8, p. 360) (C. 1906, I. 443).

Octomethylene glycol, *αθ-Octanediol,* $HO[CH_2]_8OH$, m.p. 60°, b.p. 162°/10 mm.

Nonamethylene glycol, *αι-Nonanediol,* $HO[CH_2]_9OH$, m.p. 45°, b.p. 177°/15 mm.

Decamethylene glycol, *ακ-Decanediol,* $HO[CH_2]_{10}OH$, m.p. 70°, b.p. 179°/15 mm. These glycols are obtained from dicarboxylic esters or amides by reduction (mode of formation 6*b*, p. 360) (C. 1904, I. 1399 ; 1905, II. 1701).

Higher diprimary glycols, see Monatsh. **43**, 589.

B. UNSATURATED GLYCOLS. OLEFINIC GLYCOLS

The simplest representatives possible theoretically are not known, and probably are, like vinyl alcohol, not capable of existing.

See p. 369, upon the view of furfuran as an oxide of an unknown, unsaturated glycol. See also acetonylacetone (p. 405).

iso*Dipropionyl,* iso*dibutyryl,* iso*di*iso*butyryl,* and iso*di*iso*valeryl* are olefine glycol derivatives. They result from the action of metallic sodium on an ethereal solution of propionyl chloride, butyryl chloride, *iso*butyryl chloride, and *iso*valeryl chloride. They are esters of alkylacetylene glycols (Klinger and Schmitz, Ber. **24**, 1271 : Ber. **28**, R. 1000 : J. pr. Chem. [2], **63**, 364).

Diethylacetylene glycol dipropionate, "*Dipropionyl,*" $EtOCO{\cdot}CEt:CEt{\cdot}OCOEt$, b.p. 108°/10 mm.

Dipropylacetylene glycol dibutyrate, "*Dibutyryl,*" $PrCOO{\cdot}CPr{\cdot}CPr{\cdot}OCOPr$, b.p. 119–130°/12 mm.

When these esters are hydrolysed, the corresponding keto-alcohols, propioin and butyroin are produced, and conversely the acetate $CH_3{\cdot}C(OAc) : C(OAc){\cdot}CH_3$ is produced when the sodium derivative of acetoin is treated with acetyl chloride (see p. 394).

$\Delta^{\alpha\epsilon}$-**Hexadiene-$\gamma\delta$-diol** (*Divinylethylene glycol*), $[CH_2 : CH\cdot CH(OH)\cdot]_2$, b.p. 101°/15 mm., and $\Delta^{\beta\zeta}$-**octadiene-$\delta\epsilon$-diol** (*dipropenylethylene glycol*), $[CHMe : CH\cdot CH(OH)\cdot]_2$, b.p. 121°/1 mm., are produced by the reduction of acrolein and crotonaldehyde with copper-zinc cokple and dilute acetic acid (Ann. Chim. Phys. [6], **26**, 367 : C. 1899, II, 90).

Acetylenic Glycols.—1 : 4-Acetylenic glycols are produced by the action of di-magnesium acetylene bromide on aldehydes and ketones (Ann. Chim. Phys. [8] **30**, 485) :

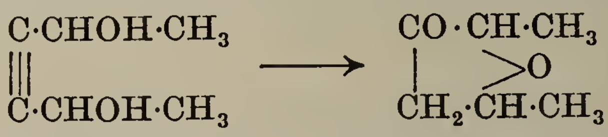
$$BrMg\cdot C \vdots C\cdot MgBr + 2CH_3CHO \longrightarrow CH_3\cdot CH(OH)\cdot C \vdots C\cdot CH(OH)\cdot CH_3.$$

$\alpha\delta$-Butinenediol, $CH_2OH\cdot C \vdots C\cdot CH_2OH$, m.p. 58°. Its *dimethyl ether*, b.p. 158°, is obtained from monochloromethyl ether and acetylene dimagnesium bromide (C. 1908, I. 1642).

Δ^{γ}-**Hexinene-$\beta\epsilon$-diol,** $MeCH(OH)\cdot C \vdots C\cdot CHMeOH$, occurs in two stereoisomeric forms, m.pp. 42° and 70°.

$\beta\epsilon$-Dimethyl-Δ^{γ}-hexinene-$\beta\epsilon$-diol, $CMe_2OH\cdot C \vdots C\cdot CMe_2OH$, m.p. 95°.

The acetylenic glycols when treated with dehydrating agents do not yield cyclic oxides, but pass over into olefine-acetylenes. They undergo isomeric change to keto-hydrofurfurans when treated with aqueous mercuric sulphate :



$$\begin{array}{l} C\cdot CHOH\cdot CH_3 \\ ||| \\ C\cdot CHOH\cdot CH_3 \end{array} \longrightarrow \begin{array}{l} CO\cdot CH\cdot CH_3 \\ |\quad\; >O \\ CH_2\cdot CH\cdot CH_3 \end{array}$$

The acetylenic glycols are reduced to the corresponding paraffin glycols by hydrogen and finely divided platinum (p. 359 : *cf.* C. 1914, I. 1813).

The diacetylenic glycols, **$\alpha\zeta$-hexadiinenediol,** $[CH_2OH\cdot C \vdots C\cdot]_2$, m.p. 111°, and **$\beta\eta$-octadiinenediol,** $[Me\cdot CHOH\cdot C \vdots C\cdot]_2$, m.p. 68°, are obtained by oxidizing the copper salts of propargyl alcohol and methylacetylenylcarbinol (p. 152) with potassium ferricyanide (C. 1897, I. 281 : II. 183).

GLYCOL DERIVATIVES

1. ETHERS OF THE GLYCOLS

A. Alkyl Ethers

The **alkyl ethers** of the glycols are prepared (1) from the metallic glycolates and alkyl iodide :

$$HO\cdot CH_2\cdot CH_2\cdot ONa + C_2H_5I = NaI + HO\cdot CH_2\cdot CH_2\cdot OC_2H_5$$
$$C_2H_4(ONa)_2 + 2C_2H_5I = 2NaI + C_2H_4(OC_2H_5)_2.$$

(2) The monoalkyl ethers of ethylene glycol result from the combination of ethylene oxide and alcohols.

(3) Dialkyl ethers can be obtained synthetically by means of the methods of formation 7 and 8 (p. 360) :

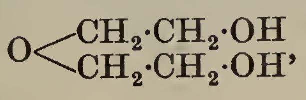
(*a*) From halogen-substituted ethers $RO[CH_2]_nX$ and Na or Mg ;
(*b*). From ketones with chloromethyl alkyl ethers and magnesium ;
(*c*) From alkoxy ketones and alkoxycarboxylic esters with magnesium alkyl halides.
(*d*) From alkoxy fatty acid salts by electrolysis.

Hydriodic acid decomposes the neutral ethers into iodoalkyls and glycols (Ber. **26**, R. 719), which are converted into alkylene iodides by excess of HI. Hydrobromic acid in the cold converts glycol dialkyl ethers into the bromohydrins of the mono-alkyl ether, $RO[CH_2]_nBr$ (C. 1904, I. 1400).

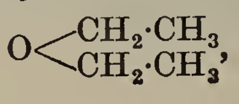
The mono-alkyl ethers of tertiary- primary 1 : 2-glycols are changes into aldehydes by the action of anhydrous formic or oxalic acid (comp. p. 361).

Glycol monoethyl ether, b.p. 127° (Ber. **35**, 3299). *Glycol diethyl ether,* b.p. 123°.

The polyethylene alcohols are most closely related to the alcohol ethers. They have been already considered after ethylene glycol (p. 363). Diethylene glycol bears the same relation to glycol as ethyl ether to ethyl alcohol :



$O<\begin{matrix}CH_2\cdot CH_2\cdot OH \\ CH_2\cdot CH_2\cdot OH\end{matrix}$, Diethylene glycol



$O<\begin{matrix}CH_2\cdot CH_3 \\ CH_2\cdot CH_3\end{matrix}$, Ethyl ether.

B. Cyclic Ethers (Alkylene Oxides)

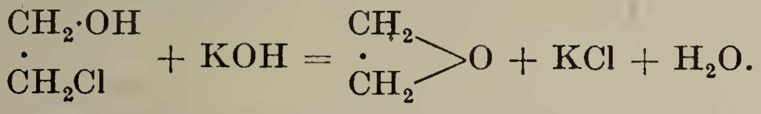
Diethylene oxide, $O<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>O$, m.p. 9°, b.p. 102°, is obtained from the red, crystalline bromine addition product of ethylene oxide, $(C_2H_4O)_2Br_2$, m.p. 65°, b.p. 95°, when it is treated with mercury. It is also prepared by heating glycol with concentrated sulphuric acid (p. 362). It unites with bromine, forming the above-mentioned *dibromide*; with iodine, to a *diiodide*, m.p. 85°; and with sulphuric acid it forms a *sulphate*, m.p. 101°. Thus, it forms double compounds or oxonium salts similar to those of the simple ethers (p. 156) (C. 1907, I. 1103). It is decomposed into acetaldehyde and glycol when heated with sulphuric acid (p. 362).

Ethylene methylene ether, *Glycol methylene acetal*, $\begin{matrix}CH_2\cdot O\\ \cdot\\ CH_2\cdot O\end{matrix}>CH_2$ b.p. 78°, is obtained from trioxymethylene, ethylene glycol and ferric chloride (Ber. **28**, R. 109), or syrupy phosphoric acid (C. 1899, I. 919). Also from glycol, formaldehyde and hydrochloric acid (C. 1900, II. 1261). **Ethylene ethylidene ether,** $\begin{matrix}CH_2\cdot O\\ CH_2\cdot O\end{matrix}>CH\cdot CH_3$, b.p. 82·5°, results from the union of ethylene oxide and acetaldehyde (comp. p. 362).

Diethylene oxide is a cyclic double ether. For the preparation of this class of substance some 1 : 3-glycols seem also to be suitable (Monatsh. **23**, 67). Simple cyclic ethers or glycol oxides are also known; and a third ether, ethylene oxide $\begin{matrix}CH_2\\ CH_2\end{matrix}>O$ (Wurtz), is also derived from glycol.

The simple cyclic ethers of the glycols, the alkylene oxides, are readily produced in various ways, depending upon whether the two OH-groups are attached to adjacent carbon atoms or not. Alkylene oxides, in which the O-atoms are in union with adjacent carbon atoms, are termed the α-alkylene oxides, whilst the others are the β-, γ-, δ-alkylene oxides.

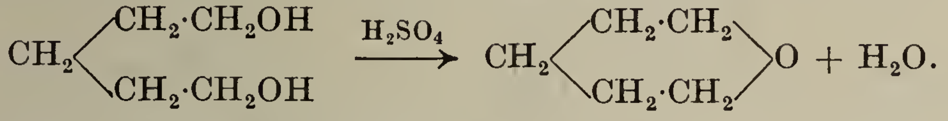
(1) Ethylene oxide itself and the ethylene oxides, as well as the β-alkylene oxides (trimethylene oxide), are prepared by the action of potassium hydroxide on the chlor- or brom-hydrins, the monohaloid esters of the respective glycols:



$$\begin{matrix}CH_2\cdot OH\\ \cdot\\ CH_2Cl\end{matrix} + KOH = \begin{matrix}CH_2\\ \cdot\\ CH_2\end{matrix}>O + KCl + H_2O.$$

(2) α-Alkylene oxides are also obtained by the oxidation of olefines by benzoyl peroxide or benzoyl hydroperoxide in inert solvents (Ber. **42**, 4811: C. 1911, I. 1280) (*cf.* p. 106).

(3) The γ- and δ-alkylene oxides (and some β-derivatives) are formed when the glycols are heated with sulphuric acid (Ber. **18**, 3285: **19**, 2843: Monatsh. **23**, 67):

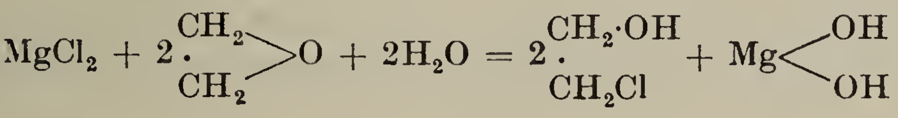


$$CH_2<\begin{matrix}CH_2\cdot CH_2OH\\ CH_2\cdot CH_2OH\end{matrix} \xrightarrow{H_2SO_4} CH_2<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>O + H_2O.$$

The α-glycols, under like treatment, lose water and yield either aldehydes or ketones, depending upon their constitution (pp. 361, 227, 256).

The ethylene oxide ring is easily ruptured, hence ethylene oxide enters into addition reactions quite as freely as its isomer acetaldehyde. The rings of tetra- and pentamethylene oxides, however, are far more stable. These can only be broken up by the halogen acids.

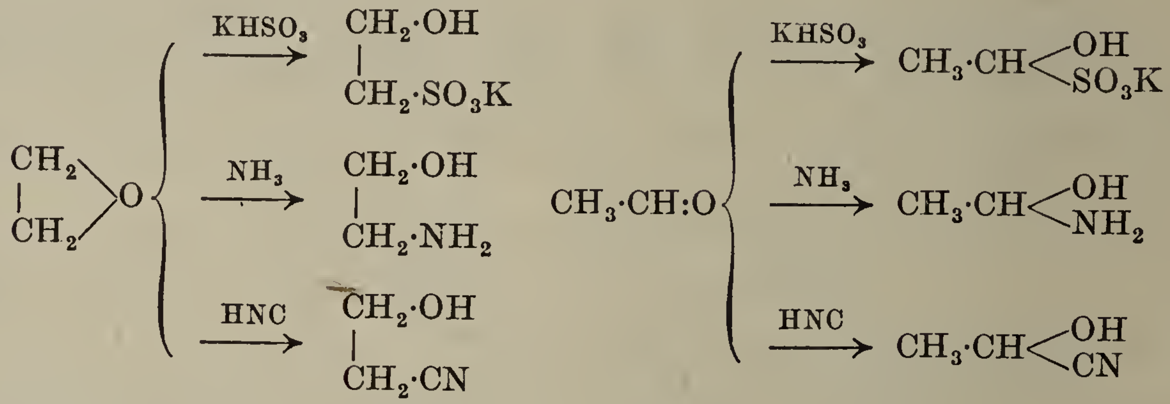
Ethylene oxide, $\begin{matrix}CH_2\\ \cdot\\ CH_2\end{matrix}>O$, b.p. 12·5°, $D._0 = 0{\cdot}898$, isomeric with acetaldehyde, $CH_3\cdot CHO$, is a pleasantly-smelling, ethereal, mobile liquid, with a neutral reaction, yet able gradually to precipitate metallic hydroxides from many metallic salts.



$$MgCl_2 + 2\begin{matrix}CH_2\\ \cdot\\ CH_2\end{matrix}>O + 2H_2O = 2\begin{matrix}CH_2\cdot OH\\ \cdot\\ CH_2Cl\end{matrix} + Mg<\begin{matrix}OH\\ OH\end{matrix}$$

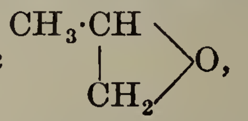
Ethylene oxide is characterized by its additive power. (1) It combines with water and slowly yields glycol. (2) Nascent hydrogen converts it into ethyl alcohol. (3) The halogen acids unite with it to form halogenhydrins, the monohaloid esters of the glycols ; hydrofluoric acid is, however, an exception (C. 1903, I. 11). (4, *a*) With alcohol it yields glycol monoethyl ether ; (*b*) with glycol it forms diethylene glycol ; (*c*) and with the latter it combines to triethylene glycol. (5) It forms ethylene alkylidene ethers (p. 367) with aldehydes. (6) Acetic acid and ethylene oxide form glycol monoacetate, and (7) with acetic anhydride the product is glycol diacetate. (8) Sodium bisulphite changes it to sodium isethionate. (9) Ammonia changes ethylene oxide to hydroxyethylamine. (10) With hydrocyanic acid it forms the nitrile of hydracrylic acid. (11) Ethylene oxide unites with sodium malonic ester (see Hydroxethylmalonic ester). Potassium hydroxide polymerizes ethylene oxide at 50–60° (Ber. **28**, R. 293).

For comparison, the following additive reactions of ethylene oxide and aldehyde are arranged side by side :

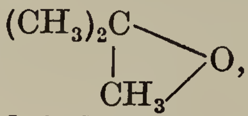


Ethylene oxide and magnesium alkyl halides form addition compounds, which are converted by heat into primary alcoholates, RCH_2CH_2OMgX (p. 134).

Higher alkylene oxides. *α-Propylene oxide*



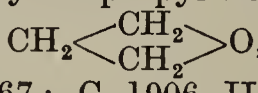
$\begin{matrix} CH_3{\cdot}CH \\ | \\ CH_2 \end{matrix}\!>O$, b.p. 35°. *iso-Butylene oxide,*



$\begin{matrix} (CH_3)_2C \\ | \\ CH_2 \end{matrix}\!>O$, b.p. 51–52°. sym.-*Dimethylethylene oxide,* b.p. 56–57°. sym.-*Methylethylethylene oxide,* b.p. 80°. iso*Propylethylene oxide,* b.p. 82°. *Trimethylethylene oxide,* b.p. 75–76°. *Tetramethylethylene oxide,* b.p. 91·7°, is produced from tetramethylethylene bromide by PbO and water (C. 1902, I. 628). It unites with water to form pinacone with considerable evolution of heat (p. 363).

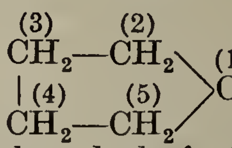
Heated to 200–260° with Al_2O_3 or other contact substances, ethylene oxide, propylene oxide and *iso*butylene oxide are transformed into the isomeric aldehydes, acetaldehyde, propionaldehyde, *iso*butylaldehyde, whilst trimethylethylene oxide gives methyl *iso*propyl ketone (Ber. **36**, 2016).

Trimethylene oxide,



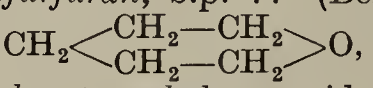
$CH_2<^{CH_2}_{CH_2}>O$, b.p. 50° ; preparation, see p. 367 ; *homologues* (Monatsh. **23**, 67 : C. 1906, II. 1179).

Tetramethylene oxide, *Tetrahydrofurfuran,*



$\begin{matrix} \overset{(3)}{CH_2}-\overset{(2)}{CH_2} \\ |\,{\scriptstyle(4)} \quad {\scriptstyle(5)} \\ CH_2-CH_2 \end{matrix}\!>\overset{(1)}{O}$, b.p. 57° (Ber. **25**, R. 912). *βε-Hexylene oxide,* 2 : 5-*Dimethyltetrahydrofurfuran,* b.p. 93° (Ber. **35**, 1336). *αα-Dimethyltetramethylene oxide,* b.p. 98° (C. 1907, I. 708). 2 : 2 : 5 : 5-*Tetramethyltetrahydrofurfuran,* b.p. 113°. *Diïsoamylene oxide,* 2 : 5-*Dimethyl*-2 : 5-*diethyltetrahydrofurfuran,* b.p. 160° (C. 1899, I. 774, 775). *γ-Pentylene oxide,* 2-*Methyltetrahydrofurfuran,* b.p. 77° (Ber. **22**, 2571).

Pentamethylene oxide,

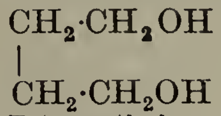


$CH_2<^{CH_2-CH_2}_{CH_2-CH_2}>O$, b.p. 82° (Ber. **27**, R. 197).

δ-Hexylene oxide, *α-Methylpentamethylene oxide,* b.p. 104°, does not unite with ammonia (Ber. **18**, 3283).

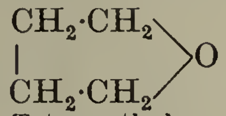
The higher polymethylene glycols are converted into their oxides only with difficulty, and form, irrespective of the relative positions of the hydroxyl groups, γ- and δ-oxides through an intramolecular isomeric change.

Note.—**Furfuran** corresponds with tetramethylene oxide. It may be considered as the cyclic ether of an unknown, unsaturated glycol.

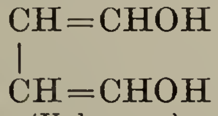


$$\begin{array}{l} CH_2{\cdot}CH_2OH \\ | \\ CH_2{\cdot}CH_2OH \end{array}$$

Tetramethylene glycol.

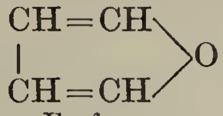


Tetramethylene oxide.



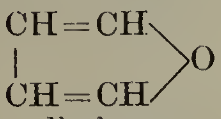
$$\begin{array}{l} CH{=}CHOH \\ | \\ CH{=}CHOH \end{array}$$

(Unknown.)

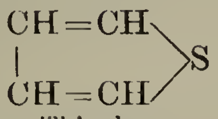


Furfuran.

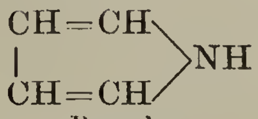
By the substitution of sulphur and of the NH-group for oxygen in furfuran *Thiophen* and *Pyrrole* are produced.



Furfuran.



Thiophen.



Pyrrole.

These compounds and their derivatives are discussed in a later volume among the heterocyclic compounds.

2. ESTERS OF THE GLYCOLS

A. Esters of Inorganic Acids

(*a*) **Halogen Esters of the Glycols.**—The glycols and monobasic acids yield neutral and basic esters. The dihalogen substitution products of the paraffins are the neutral or secondary halogen esters of the glycols. The halogen atoms in them are attached to different carbon atoms. They are isomeric with the corresponding aldehyde halides (p. 243) and the ketone halides (p. 266).

The primary haloid esters of the glycols are the *halohydrins.* These are obtained:

(1) When the glycols are treated with hydrochloric and hydrobromic acids:

$$\begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array} + HCl = \begin{array}{l} CH_2OH \\ | \\ CH_2Cl \end{array} + H_2O.$$

When heated with HI, reduction occurs simultaneously. Ethyl iodide (p. 161) is obtained from ethylene glycol. The iodohydrins can be obtained from the corresponding chloro- or bromo- compounds by the action of sodium iodide.

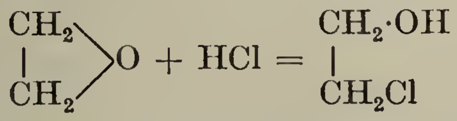
The fluorohydrins are obtained from the chloro- or bromohydrins by the action of silver or mercury fluorides (Bull. Acad. Roy. Belgique (Sci.) **1914,** 7).

By the action of hydrobromic acid on neutral glycol ethers in the cold, the ethers of the bromohydrins are obtained.

(2) They are obtained also by the direct addition of hypochlorous acid to the olefines, whereby the OH group becomes attached to the carbon atom poorest in hydrogen (J. pr. Chem. [2] **64,** 102, 387: comp. C. 1902, I. 1316):

$$\begin{array}{l} CH_2 \\ \| \\ C(CH_3)_2 \end{array} + HOCl = \begin{array}{l} CH_2Cl \\ | \\ C(CH_3)_2OH. \end{array}$$

(3) By the action of halogen acids on ethylene oxide and its homologues:



$$\begin{array}{l} CH_2 \\ | \\ CH_2 \end{array}\!\!>O + HCl = \begin{array}{l} CH_2{\cdot}OH \\ | \\ CH_2Cl \end{array}$$

(4) Synthetically, they can be prepared from halogen ketones or halogen carboxylic esters and alkyl magnesium halides (Ber. **39,** 225, 3678: C. 1906, I. 1584, II. 1179), *e.g.*:

$$CH_3{\cdot}CO{\cdot}CH_2Cl \longrightarrow (CH_3)_2C(OH){\cdot}CH_2Cl.$$

Ethers of the chlorohydrins are similarly obtained by the action of zinc alkyls or magnesium alkyl halides on $\alpha\beta$-dichloro ethers, the α-chloro atom alone being attacked by the organo-metallic compound (Ber. **40,** 4992):

$$CH_2Cl{\cdot}CHCl{\cdot}OEt \xrightarrow{MgEtI} CH_2Cl{\cdot}CH(C_2H_5){\cdot}OEt.$$

(5) Chlorohydrins are obtained from the unsaturated hydrocarbons by the action of monochlorocarbamide in dilute acetic acid solution (Bull. Soc. Chim. [4] **31,** 102).

Ethylene chlorohydrin (*glycol chlorohydrin*), $CH_2Cl{\cdot}CH_2OH$, b.p. 128°. Ethylene *bromohydrin*, b.p. 150°, and *iodohydrin*, b.p. 78°/16 mm., are obtained by warming glycol bromoacetin and iodoacetin (p. 373) with methyl alcohol (C. 1901, I. 1356). The iodohydrin is smoothly converted into acetaldehyde by warming with lead hydroxide (C. 1900, II. 31). The *fluorohydrin* is obtained by warming the bromoacetin with mercuric fluoride, followed by hydrolysis.

Trimethylene chlorohydrin (*γ-chloropropyl alcohol, γ-chloro-α-propanol*), $CH_2Cl{\cdot}CH_2{\cdot}CH_2OH$, b.p. 160°, is obtained from the glycol and hydrochloric acid.

α-Propylene glycol α-chlorohydrin, $CH_3CH(OH)CH_2Cl$, b.p. 127°, is prepared from allyl chloride by dilute sulphuric acid or by the addition of HClO to propylene: **α-propylene glycol β-chlorohydrin**, $CH_3CHCl{\cdot}CH_2OH$, b.p. 134° (C. 1903, II. 486).

*iso***Butylene glycol α-chlorohydrin**, $(OH)C(CH_3)_2CH_2Cl$, b.p. 129°, is obtained from chloroacetone or monochloroacetic acid by $Mg(CH_3)I$; also from *iso*butylene and HClO (C. 1902, I. 1093). *iso*Butylene oxide and HCl gives a mixture of this chlorohydrin and iso*butylene glycol β-chlorohydrin*, $(CH_3)_2CCl{\cdot}CH_2OH$, which easily passes into *iso*butylaldehyde (Ber. **39**, 2789, 3678).

The primary haloid esters can also be considered as substitution products of the monohydric alcohols. Glycol chlorohydrin would be chloroethyl alcohol. (1) Nascent hydrogen converts them into *primary alcohols*. (2) Oxidizing agents convert them into *halogen fatty acids*, *e.g.*, glycol chlorohydrin yields monochloroacetic acid. (3) They form alkylene oxides, and also aldehydes, under the influence of alkalis. (4) Mono- esters of the glycols are produced when they combine with salts of organic acids; *e.g.*, glycol chlorohydrin and potassium acetate yield glycol mono-acetate, $CH_3COO{\cdot}CH_2{\cdot}CH_2OH$. (5) Potassium cyanide changes them to nitriles of the hydroxyacids.

The ethers of the glycol bromo- and iodohydrin can be employed in the building up of the neutral dialkyl ethers of the higher glycols (comp. p. 360).

In close relation to the halohydrins stand certain substances produced by the action of mercury salts on ethylene (p. 104), such as *β-iodomercuriethanol*, $HOCH_2{\cdot}CH_2HgI$, and *di-β-iodomercuriethyl ether*, $O(CH_2CH_2HgI)_2$. Iodine converts them to glycol iodohydrin (above) and β-diiodo-ether, $O(CH_2CH_2I)_2$. Alkaline stannic solutions react with mercury ether bromide producing mercury diethylene oxide, $O(CH_2{\cdot}CH_2)_2Hg$, m.p. 145°, a very stable compound, which requires fuming hydrochloric acid to decompose it, generating ethylene (Ber. **33**, 1641: **34**, 1385, 2910).

The **dihalogen esters** of the glycols are very important parent bodies for the preparation of the glycols (comp. methods 1 and 4 for the formation of glycols, p. 359).

Methods of Formation.—(1) By the addition of halogens to the olefines—*e.g.* ethylene gives rise to ethylene chloride, bromide and iodide:

$$\begin{array}{l} CH_2 \\ \| \\ CH_2 \end{array} + X_2 = \begin{array}{l} CH_2X \\ | \\ CH_2X \end{array} \quad ; \quad (X = Cl,\ Br,\ I)$$

(2) By substitution of paraffins and monohalogen paraffins:

$$CH_3{\cdot}CH_3 \xrightarrow{Cl_2} CH_3{\cdot}CH_2Cl \xrightarrow[(Fe)]{Cl_2} CH_2Cl{\cdot}CH_2Cl.$$

(3) By the addition of halogen acids to monohalogen olefines. In this instance much will depend on the temperature, concentration, and other conditions, as to whether both or only one of the two possible isomers is formed:

$$CH_3{\cdot}CHBr_2 \xleftarrow{\text{dil. HBr}} CH_2:CHBr \xrightarrow{\text{Conc. HBr}} CH_2Br{\cdot}CH_2Br.$$

(4) By the action of HCl, HBr or HI on glycols and glycol halohydrins. The second OH group will be replaced with more difficulty,

and at a higher temperature, than the first. Similarly, the glycol ethers (p. 366) are converted into the dihalides by an excess of halogen acid.

(5) Alkylene diamines or halogen alkyl monoamines yield alkylene dihalides, either by the action of nitrosyl chloride or bromide (C. 1899, I. 25); or better by warming the benzoyl derivative of the amine with phosphorus chloride or bromide, and distilling the resulting imide chloride or bromide (*v. Braun*, Ber. **38,** 2346: **39,** 4112: **45,** 1970):

$$(CH_2)_n(NH\cdot COC_6H_5)_2 \longrightarrow (CH_2)_n(N:CClC_6H_5)_2 \longrightarrow (CH_2)_nCl_2 + 2NC\cdot C_6H_5$$

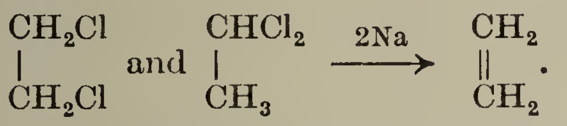
The benzoyl derivatives of the cyclic imines, such as benzoyl piperidine, benzoylpyrrolidine (comp. p. 386), yield dichloro- and dibromo-paraffins and benzonitrile by breakage of the ring, under the action of PCl_5 or PBr_5. This constitutes a convenient method of preparing αε-dichloro- and dibromopentane.

(6) By the action of PCl_5 on glycols:

(7) The chlorides and iodides can be obtained from the bromides by the action of mercuric chloride or potassium iodide respectively.

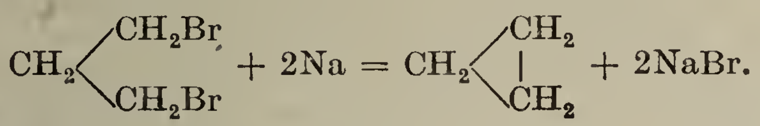
Properties.—The simple dichloro- and dibromo-esters of the glycols, or olefine dichlorides and dibromides, volatilize without decomposition. The di-iodides decompose readily in the light, and when distilled break down into olefines and iodine. The ethylene dihalides have a very sweet, pleasant odour.

Reactions.—(1) The dihalogen paraffins are converted into olefines by sodium:



$$\begin{array}{c}CH_2Cl\\ |\\ CH_2Cl\end{array} \text{ and } \begin{array}{c}CHCl_2\\ |\\ CH_3\end{array} \xrightarrow{2Na} \begin{array}{c}CH_2\\ \|\\ CH_2\end{array}.$$

*cyclo*Paraffins, such as *cyclo*propane, methyl*cyclo*butane and *cyclo*hexane, can also be obtained from dihalogen compounds and sodium (Monatsh. **3,** 625: J.C.S. **53,** 201: **65,** 599), *e.g.*:



$$CH_2\begin{cases}CH_2Br\\ CH_2Br\end{cases} + 2Na = CH_2\begin{cases}CH_2\\ |\\ CH_2\end{cases} + 2NaBr.$$

(2) Nascent hydrogen converts both di- and monohalogen paraffins into paraffins.

(3) When digested with alcoholic potassium hydroxide, halogen hydride is split off, and monohalogen olefines and acetylenes or diolefines result (pp. 111, 115).

(4) Suitable reagents change dihalogen paraffins into the corresponding glycols (p. 358) or their esters. Heating with water produces first the monohalogen hydrins of the glycols, and finally ketones and aldehydes. The 1 : 4- and 1 : 5-dihalides yield also cyclic oxides (comp. Monatsh. **23,** 64: C. 1902, I. 628: II. 19: 1903, I. 384).

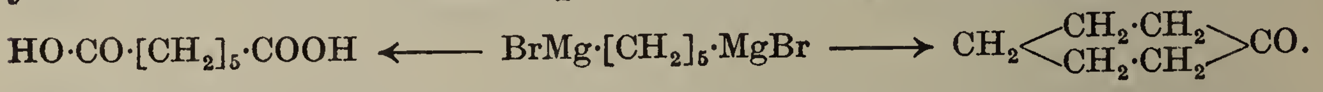
(5) Ammonia produces alkylene diamines.

(6) Potassium cyanide converts them into the nitriles of halogen carboxylic acids and the dinitriles of dicarboxylic acids.

$$CH_2Br\cdot CH_2Br + 2KCN \longrightarrow CH_2(CN)\cdot CH_2(CN) \longrightarrow CH_2(COOH)\cdot CH_2(COOH)$$

(7) The reaction with magnesium, in ethereal solution, proceeds partly similarly to the reaction of the simpler halides, and partly in a more complex fashion.

Ethylene bromide and magnesium react to produce ethylene and magnesium bromide as the principal products : if the reaction is only allowed to take place slowly, the magnesium derivative $CH_2Br{\cdot}CH_2{\cdot}MgBr$ is also formed (Ber. **38**, 1296, 3259). Trimethylene bromide and magnesium yield principally *cyclo*propane, with a very small quantity of the compound $BrMg{\cdot}[CH_2]_6{\cdot}MgBr$ (Ber. **40**, 3049). αδ-Dibromobutane and αε-dibromopentane and the higher polymethylene derivatives form the normal dimagnesium compounds $BrMg{\cdot}[CH_2]_{4\text{ or }5}{\cdot}MgBr$ when the reaction is carried out carefully, but the compounds $BrMg{\cdot}[CH_2]_{8\text{ or }10}{\cdot}MgBr$ are simultaneously formed. The magnesium derivatives of the polymethylene halides are of great synthetic value. For example, pentamethylene dimagnesium bromide yields with carbon dioxide, pimelic acid and *cyclo*hexanone.



$$HO{\cdot}CO{\cdot}[CH_2]_5{\cdot}COOH \longleftarrow BrMg{\cdot}[CH_2]_5{\cdot}MgBr \longrightarrow CH_2{<}\begin{matrix}CH_2{\cdot}CH_2\\CH_2{\cdot}CH_2\end{matrix}{>}CO.$$

Ethylene Halides—**Ethylene chloride,** *elayl chloride, Oil of the Dutch chemists,* $CH_2Cl{\cdot}CH_2Cl$, m.p. −36°, b.p. 84°, $D_4 = 1{\cdot}2808$, can be prepared (Ann. **94**, 245) by conducting ethylene into a gently heated mixture of 2 parts of manganese dioxide, 3 parts of sodium chloride, 4 parts of water and 5 parts of sulphuric acid. It is also obtained from ethylenediamine and NOCl ; also from dibenzoylethylenediamine and PCl_5 (comp. p. 371). It is insoluble in water, has an agreeable odour, and sweet taste.

Ethylene bromide, $CH_2Br{\cdot}CH_2Br$, m.p. 9°, b.p. 131°, is formed when ethylene is introduced into bromine (Ann. **168**, 64). It is also produced when ethyl bromide, bromine and iron wire are heated to 100° (Ber. **24**, 4249).

Ethylene iodide, $CH_2I{\cdot}CH_2I$, m.p. 81°, is formed on conducting ethylene into a paste of iodine and ethyl alcohol (Jahresb. **1864**, 345).

History of the Alkylene Halides.—The four Dutch chemists, *Deiman, Paets van Troostwyk, Bondt and Lauwerenburgh,* while studying the action of chlorine on ethylene, first obtained ethylene chloride in 1795 as an oily reaction product. Hence they called ethylene " gaz huileux," oily gas, a name which Fourcroy altered to " gaz olefiant," " oil-forming gas " (see *Roscoe* and *Schorlemmer*, Org. Chem., 1, 647). This phrase subsequently gave the name " *olefines* " to the series. *Balard*, the discoverer of bromine, obtained ethylene bromide in 1826 by allowing bromine to act on ethylene (Ann. Chim. Phys. [2] **32**, 375). *Faraday*, in 1821, prepared ethylene iodide by acting on ethylene with iodine in sunlight.

Propylene halides, *αβ-Dihalogen propanes,* $CH_3CHX{\cdot}CH_2X$, and **Trimethylene halides,** *αγ-Dihalogen propanes,* $CH_2X{\cdot}CH_2CH_2X$. The propylene halides result from the addition of halogens to propylene, and halogen acids to allyl halides at 100°. Trimethylene bromide is prepared from allyl bromide and hydrobromic acid at −20° and, accompanied by propylene bromide, from *cyclo*propane and bromine in hydrobromic acid (C. 1899, I. 731 : 1900, II. 465). $HgCl_2$ and KI change trimethylene bromide into the chloride and iodide.

Propylene	chloride, b.p. 97° ;	Trimethylene	chloride, b.p. 119°.
,,	bromide, ,, 141° ;	,,	bromide, ,, 165°.
,,	iodide, decomposes ;	,,	iodide, decomposes.

αγ-Dibromobutane, $CH_3CHBr{\cdot}CH_2CH_2Br$, b.p. 147°, is obtained from β-butylene glycol (C. 1902, II. 1097).

βδ-Dibromopentane, $CH_3CHBr{\cdot}CH_2CHBrCH_3$, b.p. 63°/9 mm. (C. 1904, I. 1327).

Tetramethylethylene chloride, $(CH_3)_2CCl{\cdot}CCl(CH_3)_2$, m.p. 159°, is prepared from pinacone and HCl (C. 1900, II. 1061). *Tetramethylethylene bromide,* m.p. 149°, (decomp.), results from the action of sunlight on the nitrosobromide, $(CH_3)_2CBr{\cdot}C(NO)(CH_3)_2$. This substance is prepared from tetramethylethylene and NOBr (comp. p. 377) (Ber. **37**, 545). It is a very volatile blue crystalline powder.

Higher Homologues of the Polymethylene Halide Series are mostly obtained by the general methods of preparation, Nos. 4 and 5 (p. 370) (J. pr.

Chem. [2] **39**, 542: Ber. **27**, R. 735: **38**, 2346: **39**, 1112: C. 1903, I. 583: 1904, II. 429: 1905, I. 1698: 1906, I. 443).

Tetramethylene chloride, $Cl[CH_2]_4Cl$, b.p. 162°; *bromide*, m.p. $-20°$, b.p. 82°/12 mm.; *iodide*, m.p. 5·8°.

Pentamethylene chloride, $Cl[CH_2]_5Cl$, b.p. 177°; *bromide*, b.p. 221°; *iodide*, m.p. 9°, b.p. 149°/20 mm.

Hexamethylene chloride, $Cl[CH_2]_6Cl$, b.p. 204°; *iodide*, m.p. 9·5°, b.p. 163°/17 mm.

Heptamethylene chloride, $Cl[CH_2]_7Cl$, b.p. 126°/28 mm.; *iodide*, m.p. 0°, b.p. 178°/20 mm.

βε-Dibromohexane, $CH_3CHBr{\cdot}CH_2{\cdot}CH_2{\cdot}CHBrCH_3$, is prepared from βε-hexylene glycol (p. 365), from Δ^{α}-hexene-ε-ol (butallylmethylcarbinol), or from diallyl (p. 117) by means of hydrobromic acid. A mixture of stereoisomeric forms is obtained, containing a *racemic* form, m.p. 38°, and the *meso* form, a liquid, b.p. 100°/20 mm. (Ber. **34**, 2569: **35**, 1337).

Sodium converts these compounds into *cyclo*paraffins (Vol. II), just as sodium and trimethylene bromide produce trimethylene. Sodium malonic esters, sodium acetoacetic esters, and polymethylene bromides produce *cyclo*paraffin carboxylic esters (Vol. II).

Mixed, neutral halogen esters of the glycols, containing two different halogen atoms, are also known.

(*b*) **Esters of Mineral Acids containing Oxygen.**

Ethylene nitrate, *glycol dinitrate*, $C_2H_4(O{\cdot}NO_2)_2$, $D_8 = 1{\cdot}483$, is produced on heating ethylene iodide with silver nitrate in alcoholic solution, or by dissolving glycol in a mixture of concentrated sulphuric and nitric acids:

$$C_2H_4(OH)_2 + 2HO{\cdot}NO_2 = C_2H_4(O{\cdot}NO_2)_2 + 2H_2O.$$

This reaction is characteristic of all hydroxyl compounds (polyhydric alcohols and polyhydroxy acids).

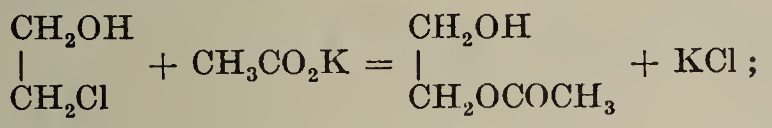
The nitrate is a yellowish liquid, insoluble in water. It explodes when heated (like nitroglycerine). Alkalis saponify the ester with formation of nitric acid and glycol.

Glycolsulphuric acid, $C_2H_4(OH){\cdot}SO_4H$, is produced on heating glycol with sulphuric acid. It is similar to ethylsulphuric acid (p. 168), and decomposes, when boiled with water or alkalis, into glycol and sulphuric acid.

B. Esters of Carboxylic Acids

The esters of the fatty acids with dihydric alcohols or glycols are obtained by methods already described:—

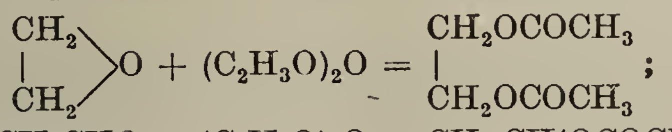
(1) From the haloid esters of the glycols: (halogenohydrins and alkylene halides) with salts of fatty acids:



$$\begin{array}{l}CH_2OH\\ |\\ CH_2Cl\end{array} + CH_3CO_2K = \begin{array}{l}CH_2OH\\ |\\ CH_2OCOCH_3\end{array} + KCl;$$

(2) From glycols by means of free acids, acid chlorides or acid anhydrides.

(3) They are also obtained by the direct addition of acid anhydrides to ethylene oxides, similarly to the formation of the alkylidene esters from aldehydes and acid anhydrides (p. 244):



$$\begin{array}{l}CH_2\\ |\\ CH_2\end{array}\!\!>O + (C_2H_3O)_2O = \begin{array}{l}CH_2OCOCH_3\\ |\\ CH_2OCOCH_3\end{array};$$

$$CH_3CHO + (C_2H_3O)_2O = CH_3{\cdot}CH(OCOCH_3)_2.$$

Glycol diformin, $C_2H_4(O{\cdot}CHO)_2$, b.p. 89°/25 mm., is prepared from glycol by a mixture of formic acid and acetic anyhydride (C. 1900, II. 314).

Glycol monoacetate, $CH_2(OH)CH_2OCOCH_3$, b.p. 182°, is a liquid miscible with water. If hydrochloric acid gas be led into the warmed substance there is formed *glycol chloroacetin*, *chloroethyl acetate*, $CH_2ClCH_2{\cdot}O{\cdot}C_2H_3O$, b.p. 144°. Similarly hydrobromic acid produces *glycol bromoacetin*, b.p. 163°, which is converted into the *iodoacetin*, b.p. 110°/60 mm., by sodium iodide and the *fluoroacetin*, b.p. 119°, by mercuric fluoride (C. 1901, I. 1356 : Bull. Acad. Roy. Belg. (Sci.) **1914**, 7).

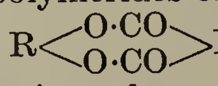
Glycol diacetate, $C_2H_4(O{\cdot}C_2H_3O)_2$, b.p. 186°, $D_0 = 1{\cdot}128$. It dissolves in 7 parts of water. **Glycol distearate**, $C_2H_4(OCOC_{17}H_{35})_2$, m.p. 79°, b.p. 241°/2 mm. **Glycol dipalmitate**, $C_2H_4(OCOC_{15}H_{31})_2$, m.p. 72°, b.p. 226°/0 mm. (Ber. **36**, 4340).

α-Propylene glycol diacetate, $CH_3{\cdot}C_2H_3(O{\cdot}COCH_3)_2$, b.p. 186°.

Trimethylene glycol diacetate, $(CH_2)_3(OCOCH_3)_2$, b.p. 210°.

The formation of the acid esters is well suited for the detection and determination of the number of hydroxyl groups in the polyhydric alcohols, the sugars and the phenols. Benzoic esters are particularly especially easy to prepare. It is only necessary to shake up the substance with benzoyl chloride and sodium hydroxide in order to benzoylate all the hydroxyls (Ber. **21**, 2744 : **22**, R. 668, 817). The formation of the nitric acid ester is also well adapted for the purpose (see Glycol dinitrate, p. 373) ; also the carbamic esters (urethanes) resulting from the action of *iso*cyanic esters (*q.v.*), especially the phenyl *iso*cyanate (*q.v.*).

For carboxylic esters of unsaturated glycols, see p. 365.

Glycol Esters of Dibasic Acids.—The glycol esters of dibasic acids such as malonic and adipic acids readily form polymerides of high molecular weight. When the number of atoms in the system  $R{<}\begin{smallmatrix}O\cdot CO\\O\cdot CO\end{smallmatrix}{>}R$ is too great to permit of the formation of a five- or six-atom ring, these polymerides are formed instead of the simple esters (J.A.C.S. **51**, 2560 : **52**, 314, etc.).

3. SULPHUR DERIVATIVES OF THE GLYCOLS

A. **Mercaptans.**—The mercaptans corresponding to ethylene glycol are obtained :

(1) by treating the halogenohydrins and olefine dihalides with potassium hydrosulphide ;

(2) by hydrolysis of the dithiourethanes obtained from olefine dihalides and ammonium dithiocarbamate (Ber. **42**, 4568) :

$$[CH_2]_x(S{\cdot}CS{\cdot}NH_2)_2 + 4KOH \longrightarrow 2KCNS + [CH_2]_x(SK)_2 + 4H_2O.$$

Monothio-ethylene glycol, $HSCH_2{\cdot}CH_2OH$, yields isethionic acid (p. 375) when treated with nitric acid.

Dithioglycol, ethylene mercaptan, dithiolethane, $C_2H_4(SH)_2$, b.p. 146°, $D = 1{\cdot}12$, possesses an odour something like that of mercaptan. It is insoluble in water and dissolves in alcohol and ether. It shows the reactions of a mercaptan (Ber. **20**, 461).

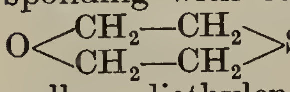
Trimethylene mercaptan, $HS(CH_2)_3SH$, b.p. 169° (Ber. **32**, 1370).

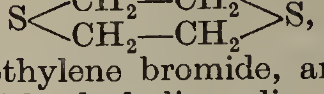
Tetramethylenedithioglycol (*αδ-dithiolbutane*), $HS{\cdot}[CH_2]_4{\cdot}SH$, b.p. 105°/30 mm.: *penta-, hexa-,* and *decamethylene dithioglycols*, b.p. 110°/16 mm., 118°/15 mm., 176°/16 mm. (m.p. 20°).

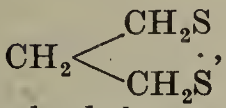
B. **Sulphides.**—(*a*) **Alkyl Derivatives of the Thioglycols.**—*Ethyl β-hydroxyethyl sulphide*, $EtS{\cdot}CH_2{\cdot}CH_2OH$, b.p. 184°.

Ethylene dimethyl sulphide, $MeS{\cdot}CH_2{\cdot}CH_2{\cdot}SMe$, b.p. 183°. *Ethylene diethyl sulphide*, b.p. 188°.

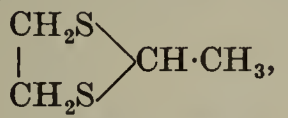
(*b*) **Vinyl Alkyl Derivatives of Dithioglycol (Sulphurans).**—*Vinyl ethyl ethylene sulphide*, $CH_2 : CH{\cdot}S{\cdot}CH_2CH_2{\cdot}SEt$, b.p. 214° (see under Sulphonium compounds, below). *Diethylthiolethylene*, $EtS{\cdot}CH : CH{\cdot}SEt$, b.p. 170°/13 mm., is obtained from dichloroethylene and ethyl mercaptan by the action of alcoholic potash (Ann. **394**, 325).

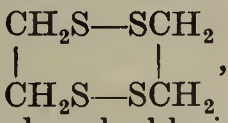
(*c*) **Thiodiglycol**, $HOCH_2CH_2{\cdot}S{\cdot}CH_2CH_2OH$, corresponding with diglycol, is also known (Ber. **19**, 3259). However, the simple ethylene sulphide, corresponding with ethylene oxide, is not known, whilst *diethylene oxide sulphone*,  $O{<}\begin{smallmatrix}CH_2-CH_2\\CH_2-CH_2\end{smallmatrix}{>}SO_2$, m.p. 130°, corresponding with diethylene oxysulphide, as well as diethylene disulphide, are known.

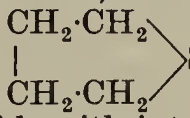
(*d*) **Cyclic sulphides** : *Diethylene disulphide*,  $S{<}\begin{smallmatrix}CH_2-CH_2\\CH_2-CH_2\end{smallmatrix}{>}S$, m.p. 112°, b.p. 200°, is formed from ethylene mercaptan, ethylene bromide, and sodium ethoxide. When ethylene bromide is digested with alcoholic sodium sulphide, a *polymeric ethylene sulphide*, $(C_2H_4S)_n$, m.p. 145°, is produced at first. This is a white, amorphous powder, insoluble in the ordinary solvents, which protracted boiling with phenol changes to diethylene disulphide (Ann. **240**, 305 : Ber. **19**, 3263 : **20**, 2967).

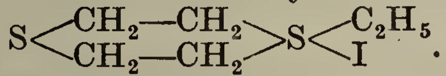
Trimethylene disulphide,  $CH_2<\begin{array}{l}CH_2S\\ \quad\,\vert\\CH_2S\end{array}$, m.p. 75° (Ber. **32**, 1370).

(*e*) *Ethylene mercaptals* and *ethylene mercaptoles* are similarly produced from ethylene mercaptan by the action of aldehydes, ketones, and HCl, just as the mercaptals (p. 247) and the mercaptoles (p. 267) are obtained from ordinary mercaptans (Ber. **21**, 1473).

Ethylene dithioethylidene,  $\begin{array}{l}CH_2S\\ \vert\\CH_2S\end{array}>CH{\cdot}CH_3$, b.p. 173°.

(*f*) *Diethylene tetrasulphide*,  $\begin{array}{lcl}CH_2S & — & SCH_2\\ \vert & & \vert\\ CH_2S & — & SCH_2\end{array}$, m.p. 150°, is produced by the action of the halogens, or sulphuryl chloride or hydroxylamine on ethylene mercaptan. It is a white, amorphous powder (Ber. **21**, 1470).

(*g*) *Tetramethylene sulphide* (*tetrahydrothiophen*),  $\begin{array}{l}CH_2{\cdot}CH_2\\ \vert\\CH_2{\cdot}CH_2\end{array}>S$, b.p. 119°, and *pentamethylene sulphide*, b.p. 141°, form mobile liquids with intolerable penetrating odours. They are obtained from tetramethylene and pentamethylene iodides and potassium sulphide (Ber. **43**, 545, 3220).

C. **Sulphonium Derivatives.**—Ethyl iodide and diethylene disulphide unite to form the *ethiodide*,  $S<\begin{array}{l}CH_2—CH_2\\CH_2—CH_2\end{array}>S<\begin{array}{l}C_2H_5\\I\end{array}$.

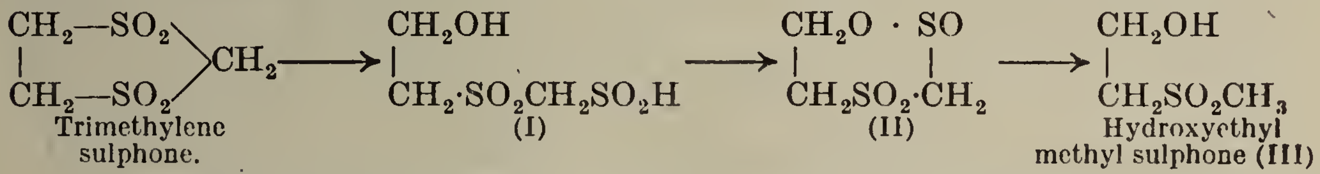
Ethyl sulphuran, $EtS{\cdot}C_2H_4{\cdot}S{\cdot}CH : CH_2$, is produced on distilling the abovementioned iodide with sodium hydroxide. The ring of diethylene disulphide is broken.

The union of the derivatives of diethylene disulphide with the higher alkyl iodides yields homologous compounds. By similar treatment these yield **sulphurans** or alkyl vinyl thio-ethers of ethylene (Ber. **19**, 3263 : **20**, 2967 : Ann. **240**, 305). (See B (*b*) above.)

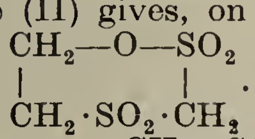
D. **Sulphones.**—The disulphones are produced when the open and the cyclic disulphides are oxidized by potassium permanganate. All sulphones, in which sulphone groups are attached to two adjacent carbon atoms, can be hydrolysed (*Stuffer's law*, Ber. **26**, 1125).

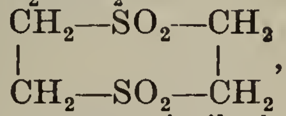
(*a*) **Open chain sulphones :** *Ethylene diethyl sulphone*, $C_2H_4(SO_2{\cdot}Et)_2$, m.p. 137°, has been obtained (1) from diethylthiolethane ; (2) from ethylene bromide by the action of sodium ethyl sulphinate, and (3) from sodium ethylene disulphinate by the action of ethyl bromide (Ber. **21**, R. 102).

(*b*) **Cyclic sulphones** (Ber. **26**, 1124 ; **27**, 3043) : *Trimethylene disulphone*, m.p. 204–205°, results from the oxidation of methylene dithioethylene. Barium hydroxide solution decomposes this into the *acid* (I). This, on boiling with water, forms first an internal *anhydride* (II), b.p. 164°, which then loses SO_2 and turns into the *sulphone* (III), m.p. 20°.



$$\begin{array}{l}CH_2—SO_2\\ \vert\\CH_2—SO_2\end{array}>CH_2 \longrightarrow \begin{array}{l}CH_2OH\\ \vert\\CH_2{\cdot}SO_2CH_2SO_2H\end{array} \longrightarrow \begin{array}{lcl}CH_2O & \cdot & SO\\ \vert & & \vert\\CH_2SO_2 & \cdot & CH_2\end{array} \longrightarrow \begin{array}{l}CH_2OH\\ \vert\\CH_2SO_2CH_3\end{array}$$

The anhydride (II) gives, on oxidation, hydroxyethyl sulphone methylene sulphone lactone,  $\begin{array}{lcl}CH_2 & —O— & SO_2\\ \vert & & \vert\\CH_2 & {\cdot}SO_2{\cdot} & CH_2\end{array}$.

Diethylene disulphone,  $\begin{array}{lcl}CH_2 & —SO_2— & CH_2\\ \vert & & \vert\\CH_2 & —SO_2— & CH_2\end{array}$, results from the oxidation of diethylene disulphide, and decomposes similarly to trimethylene disulphone.

E. **Sulphonic Acids.—Isethionic acid,** *hydroxyethanesulphonic acid*, $HO{\cdot}C_2H_4{\cdot}SO_3H$, is isomeric with ethylsulphuric acid, $C_2H_5O{\cdot}$-

SO_3H, and is produced (1) by oxidizing monothioethylene glycol with HNO_3; (2) by the action of nitrous acid on taurine or aminoisethionic acid (comp. formation of glycollic acid from glycocoll, p. 440):

$$H_2N\cdot CH_2CH_2SO_3H + HONO = HO\cdot CH_2CH_2SO_3H + N_2 + H_2O.$$

(3) by heating glycol chlorohydrin with potassium sulphite; (4) by boiling ethionic acid (p. 377) with water (Ber. **14**, 64; Ann. **223**, 198); (5) from ethylene oxide and potassium hydrogen sulphite.

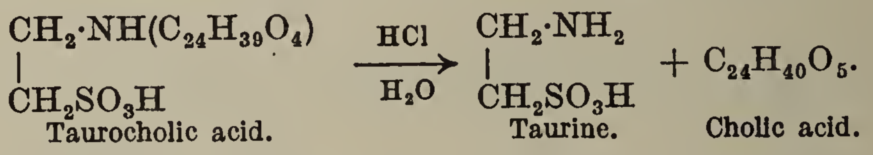
Isethionic acid is a thick liquid, which solidifies when allowed to stand over sulphuric acid. Its salts are very stable and crystallize well. Chromic acid oxidizes isethionic acid to sulpho-acetic acid.

The *barium salt* is anhydrous; *ammonium salt* forms plates, m.p. 135°, and at 210–220° it changes to the ammonium salt of *di-isethionic acid*, $O(CH_2\cdot CH_2SO_3NH_4)_2$ (Ber. **14**, 65). *Ethyl isethionate*, b.p. 120° (see Ber. **15**, 947).

PCl_5 converts the acid into *chloroethanesulphonic chloride*, $Cl\cdot CH_2CH_2SO_2Cl$, b.p. 200°. This is also formed by heating ethane disulphochloride. When it is boiled with water it is converted into *chloroethanesulphonic acid*, $CH_2Cl\cdot CH_2\cdot SO_3H$ (Ann. **223**, 212).

Taurine, *aminoisethionic acid, aminoethanesulphonic acid,* $\begin{array}{l}CH_2NH_2\\|\\CH_2\cdot SO_3H\end{array}$, or $\begin{array}{l}CH_2\cdot NH_3\\|\quad\ \ |\\CH_2\cdot SO_3\end{array}$, was discovered by *Gmelin* in 1824; its sulphur content, which had previously been overlooked, was detected in 1846 by *Redtenbacher*. It is considered in this connection because of its intimate relationship to isethionic acid. It occurs as taurocholic acid, in combination with cholic acid, in the bile of oxen (hence the name—ταῦρος, ox) and many other animals, and also in the different animal secretions. It can be obtained from the shell-fish *Haliotis*, J. Biol. Chem. **33**, 499.

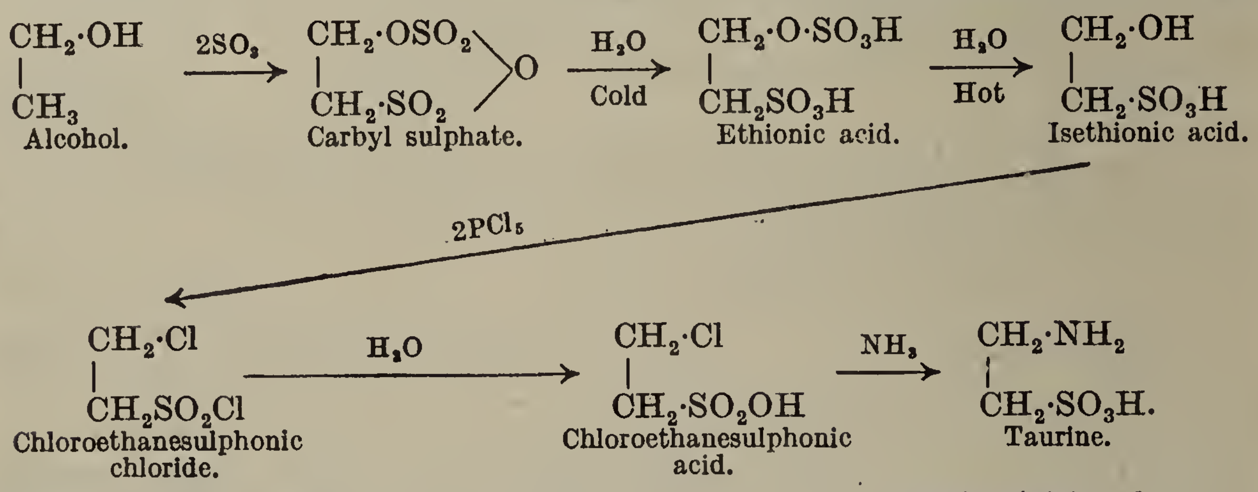
It is formed when taurocholic acid is decomposed with hydrochloric acid (*Preparation*, see Biochem. J. **21**, 1065):



$$\begin{array}{c}CH_2\cdot NH(C_{24}H_{39}O_4)\\|\\CH_2SO_3H\\\text{Taurocholic acid.}\end{array}\xrightarrow[H_2O]{HCl}\begin{array}{c}CH_2\cdot NH_2\\|\\CH_2SO_3H\\\text{Taurine.}\end{array}+\begin{array}{c}C_{24}H_{40}O_5.\\\text{Cholic acid.}\end{array}$$

It can be prepared artificially by heating chloroethanesulphonic acid, $CH_2Cl\cdot CH_2SO_3H$, with aqueous ammonia (*Kolbe*, Ann. **122**, 33).

Ethylene or ethyl alcohol combine with SO_3 to give carbyl sulphate, a derivative of isethionic acid. The following diagram shows the course of the synthesis:



$$\begin{array}{c}CH_2\cdot OH\\|\\CH_3\\\text{Alcohol.}\end{array}\xrightarrow{2SO_3}\begin{array}{c}\left.\begin{array}{l}CH_2\cdot OSO_2\\|\\CH_2\cdot SO_2\end{array}\right\rangle O\\\text{Carbyl sulphate.}\end{array}\xrightarrow[\text{Cold}]{H_2O}\begin{array}{c}CH_2\cdot O\cdot SO_3H\\|\\CH_2SO_3H\\\text{Ethionic acid.}\end{array}\xrightarrow[\text{Hot}]{H_2O}\begin{array}{c}CH_2\cdot OH\\|\\CH_2\cdot SO_3H\\\text{Isethionic acid.}\end{array}$$

$$\xrightarrow{2PCl_5}\begin{array}{c}CH_2\cdot Cl\\|\\CH_2SO_2Cl\\\text{Chloroethanesulphonic}\\\text{chloride.}\end{array}\xrightarrow{H_2O}\begin{array}{c}CH_2\cdot Cl\\|\\CH_2\cdot SO_2OH\\\text{Chloroethanesulphonic}\\\text{acid.}\end{array}\xrightarrow{NH_3}\begin{array}{c}CH_2\cdot NH_2\\|\\CH_2\cdot SO_3H.\\\text{Taurine.}\end{array}$$

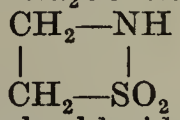
Taurine also results when ethylenimine is evaporated together with sulphurous acid.

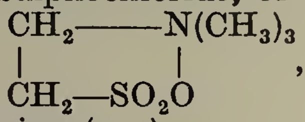
Taurine crystallizes in large, monoclinic prisms, m.p. (decomp.) c. 240°, insoluble in alcohol, but readily dissolved by hot water. It contains the groups NH_2 and SO_3H, and is, therefore, both a base and a sulphonic acid, but as the two groups neutralize each other, the compound has a neutral reaction. It may, therefore, be considered as a cyclic ammonium salt, as indicated in the second constitutional formula. It can form salts with the alkalis. It separates unaltered from its solution in acids (see Glycocoll).

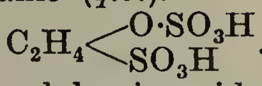
Nitrous acid converts it into isethionic acid (p. 375). Boiling alkalis and acids do not affect it, but when fused with potassium hydroxide it breaks up according to the equation :

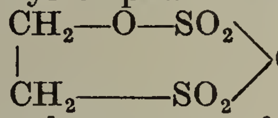
$$NH_2CH_2CH_2SO_3K + 2KOH = CH_3CO_2K + K_2SO_3 + NH_3 + H_2.$$

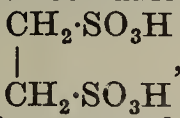
Taurine introduced into the animal economy is excreted in the urine as *taurocarbamic acid*, $NH_2CONH\cdot CH_2\cdot CH_2\cdot SO_3H$.

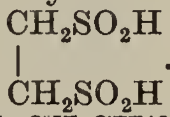
Anhydrotaurine,  $\begin{array}{l}CH_2—NH\\ |\qquad\ \ |\\ CH_2—SO_2\end{array}$, m.p. 88°, is formed by the action of ammonia on chloroethane sulphochloride, or on ethane disulphochloride (C. 1898, I. 20).

Taurobetaine,  $\begin{array}{l}CH_2——N(CH_3)_3\\ |\qquad\qquad\ \ |\\ CH_2—SO_2O\end{array}$, is prepared by methylating taurine, and is analogous to betaine (*q.v.*).

Ethionic acid,  $C_2H_4<\begin{matrix}O\cdot SO_3H\\ SO_3H\end{matrix}$. The constitution of this acid would indicate it to be both a sulphonic acid and primary sulphuric ester. It is therefore dibasic, and on boiling with water readily yields sulphuric and isethionic acids. It results when carbyl sulphate takes up water.

Carbyl sulphate,  $\left.\begin{array}{l}CH_2—O—SO_2\\ |\\ CH_2———SO_2\end{array}\right>O$, the *anhydride* of *ethionic acid* (Ann. **223**, 210), is formed when the vapours of SO_3 are passed through anhydrous alcohol. It is also produced by the direct union of ethylene with two molecules of SO_3.

Ethanedisulphonic acid,  $\begin{array}{l}CH_2\cdot SO_3H\\ |\\ CH_2\cdot SO_3H\end{array}$, m.p. 100°, may be prepared from glycol mercaptan and ethylene thiocyanate by means of concentrated nitric acid ; by the action of fuming sulphuric acid on alcohol or ether ; or by boiling ethylene bromide with a concentrated solution of potassium sulphite. It is easily soluble in water. Reduction with zinc dust, see Ber. **38**, 1071.

Ethane disulphochloride, $SO_2Cl\cdot CH_2\cdot CH_2\cdot SO_2Cl$, m.p. 98°, by the action of zinc dust, forms the zinc salt of *ethanedisulphinic acid*,  $\begin{array}{l}CH_2SO_2H\\ |\\ CH_2SO_2H\end{array}$. The disulphochloride, like the chloride of propane-$\alpha\beta$-disulphonic acid, $CH_3CH(SO_2Cl)$-CH_2SO_2Cl, m.p. 48°, easily gives up SO_2 ; whilst the chloride of *propane-$\alpha\gamma$-disulphonic acid*, $CH_2(CH_2SO_2Cl)_2$, is more stable (Ber. **34**, 3467 : **36**, 3626). This is in accordance with *Stuffer's* rule (p. 375).

4. NITROGEN DERIVATIVES OF THE GLYCOLS

A. Nitroso-compounds.

The addition-products of the olefines with nitrosyl chloride belong to this group (comp. the Terpenes, Vol. II).

Tetramethylethylene nitrosochloride, $(CH_3)_2C(NO)\cdot CCl(CH_3)_2$, m.p. 121°, is prepared by adding sodium nitrite to tetramethylethylene in an alcoholic solution of hydrochloric acid in the cold (Ber. **27**, 455 : R. 467). It has a blue colour, and a somewhat penetrating camphor-like odour.

If the nitroso group in these compounds is attached to a primary or secondary carbon atom, they readily undergo tautomeric change to *iso*nitroso-compounds, which are treated later as oximes of the nitro-ketones, e.g. :

$$Me_2C(NO_2)\cdot CH(NO)\cdot CH_3 \longrightarrow Me_2C(NO_2)\cdot C(:NOH)\cdot CH_3.$$

B. Nitro Compounds.

Only the mononitro compound derived from glycol, β-nitroethyl alcohol, is known. The nitro- derivatives of the alcohols are obtained by the interaction of silver nitrite and the halogenohydrins, and by the condensation of the primary nitroparaffins with aldehydes under the influence of dilute potassium bicarbonate or potassium hydroxide solutions (C. 1899, I. 1154).

β-Nitroethyl alcohol, $CH_2NO_2{\cdot}CH_2OH$, b.p. 120°/35 mm., forms a heavy oil (Ber. **53**, 208). *β-Nitroethyl nitrate,* $CH_2NO_2{\cdot}CH_2{\cdot}ONO_2$, b.p. 120–122°/17 mm., and *glycol dinitrate,* $CH_2(O{\cdot}NO_2){\cdot}CH_2{\cdot}ONO_2$, b.p. 105°/19 mm., are produced by the union of ethylene and nitric acid (Ber. **53**, 206).

β-Nitropropyl alcohol, $CH_3CH(NO_2)CH_2OH$, b.p. 121°/22 mm. **Nitro-*iso*propyl alcohol,** $CH_3{\cdot}CH(OH)CH_2NO_2$, b.p. 112°/30 mm., $D_{18} = 1{\cdot}191$ (Ber. **28**, R. 606) (see also Nitro-olefines, p. 182). **γ-Nitropropanol,** $HO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2NO_2$, b.p. 139°/32 mm.

For *nitro-alcohols* containing 4, 5, and 6 carbon atoms, see C. 1897, II. 337 : 1898, I. 193. For *dinitro-* and *halogen-nitro-*compounds, corresponding with the glycol series, see pp. 182, 185.

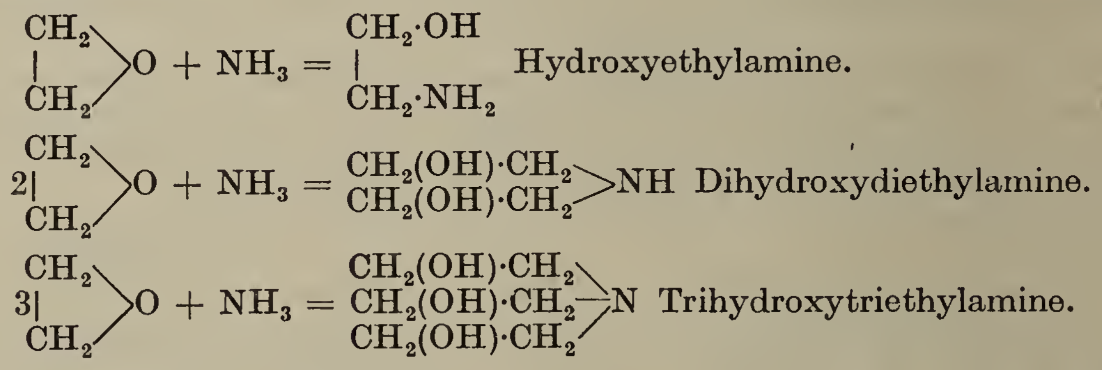
C. Amines and Ammonium Compounds of the Glycols.

There are two series of amines, derived from the glycols, and corresponding with the two series of glycolates, esters, mercaptans, etc. :

$HO{\cdot}CH_2CH_2{\cdot}OH$,	$HO{\cdot}CH_2CH_2{\cdot}NH_2$,	and	$NH_2{\cdot}CH_2CH_2{\cdot}NH_2$.
Glycol.	Hydroxyethylamine.		Ethylene diamine.

The amines of the glycols fall into two classes : (1) The hydroxyalkylamines and their derivatives ; (2) the alkylene diamines and their derivatives.

(I) **Hydroxyalkylamines** and their derivatives.—Methods of formation : (1) action of ammonia on the halohydrins ; (2) by the union of ammonia and alkylene oxides in the presence of water (Ber. **32**, 729 : C. 1900, II. 1009). In these two reactions the products are primary, secondary, and tertiary hydroxyalkyl bases, *e.g.* :

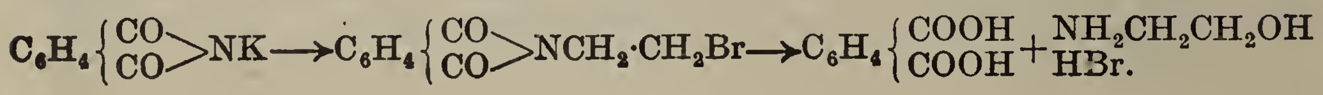


These three bases are best separated by distillation under reduced pressure (Ber. **30**, 909). They were discovered by *Wurtz* and closely investigated by *Knorr.*

(3) by reduction of nitro-alcohols (see above) hydroxyacid nitriles, amino-ketones or *iso*nitroso-ketones (Ber. **33**, 2829, 3169 : C. 1908, I. 1676) ;

(4) by the action of sulphuric acid on allylamine with addition of water (Ber. **16**, 532) ;

(5) by the application of the phthalimide reaction (p. 189). Alkylene halides are allowed to act on potassium phthalimide, the reaction-product being heated with sulphuric acid to 200–230° :



The course of the alkali hydrolysis of the bromoalkylphthalimides is discussed in Ber. **38,** 2404, etc.

The amino-alcohols are also obtained by the direct action of alkylene oxides on free phthalimide, followed by hydrolysis of the product (Ber. **50,** 819).

(6) The *dialkylamino-alcohols* (*Alkamines*) are formed by the action of secondary amines on halogenohydrins and alkylene oxides, and from dialkylaminoacetic esters, dialkylaminoketones and amino-acid esters by the action of the magnesium alkyl halides (Ber. **39,** 810: J. Pharm. Chim. [7] **2,** 56: Z. physiol. Chem. **160,** 1):

$$NEt_2{\cdot}CH_2{\cdot}COOEt \xrightarrow{MgEtI} NEt_2{\cdot}CH_2{\cdot}CEt_2OH.$$

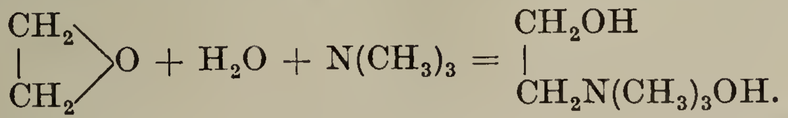
The alkamines are thick, strongly alkaline liquids which partially decompose on distillation. They are separated by fractional crystallization of their hydrochlorides and platinochlorides.

The alkamines and their carboxylic esters (*Alkeines*) frequently possess physiological activity (C. 1904, I. 1195: 1906, I. 1584). *Stovaine,* the hydrochloride of the benzoate of dimethylaminopentanol, $C_2H_5{\cdot}CMe(O{\cdot}COC_6H_5){\cdot}CH_2NMe_2,HCl$, which is used as a local anæsthetic in place of cocaine deserves mention in this connection.

Hydroxyethylamine, *cholamine, β-aminoethanol,* $CH_2OH{\cdot}CH_2{\cdot}NH_2$, b.p. 171°, and the homologous *alkamines,* $CH_2OH{\cdot}CH{\cdot}NHR$ and $CH_2OH{\cdot}CH_2{\cdot}NRR'$, are best prepared by the addition of ammonia or the appropriate amine to ethylene oxide in aqueous solution (Ann. **315,** 104: **316,** 311: C. 1908, II. 121, 1706). Hydroxyethylamine is also obtained by the putrefaction of serine (Biochem. Z. **95,** 281). *Dimethylaminoethanol,* $NMe_2CH_2{\cdot}CH_2OH$, is formed as a breakdown product of α-methylmorphimethine (see Alkaloids, Vol. III).

Choline, *hydroxyethyltrimethylammonium hydroxide, bilineurine, Sincalin,* $HOCH_2{\cdot}CH_2{\cdot}N(CH_3)_3OH$, is quite widely distributed in the animal organism, especially in the brain, and in the yolk of egg, in which it is present as *lecithin* (*q.v.*), combined with glycerophosphoric acid and fatty acids. It is present in hops, hence it occurs in beer. It has also been found in the plant, *Strophanthus.* It is obtained, also, from sinapin (the alkaloid of *Sinapis alba*), when it is boiled with alkalis (hence the name *sincalin*). It occurs, together with muscarine, $(HO)_2CHCH_2N(CH_3)_3OH$(?) (Ber. **27,** 166), in fly agaric (*Argaricus muscarius*).

History.—*A. Strecker* discovered this base (1862) in the bile of swine and oxen. He gave it the name *choline,* from χολή, bile. *Liebreich* obtained it from protagon, a constituent of the nerve substance, and at first named it *neurine,* from νεῦρον, nerve; this he later changed to *bilineurine,* to distinguish it from the corresponding vinyl base, which continued to bear the name *neurine.* The constitution of choline was explained by *Baeyer,* and *Wurtz* showed how it might be synthetically prepared by the action of trimethylamine on a concentrated aqueous solution of ethylene oxide:



$$\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!O + H_2O + N(CH_3)_3 = \begin{matrix} CH_2OH \\ | \\ CH_2N(CH_3)_3OH. \end{matrix}$$

Its hydrochloride is produced from ethylene chlorohydrin and trimethylamine. Ethylene bromide and trimethylamine at 110–120° produce bromoethyltrimethylammonium bromide, which on heating with water at 160°, gives choline hydrobromide, $HOCH_2CH_2N(CH)_3Br$ (Ber. **36**, 2901).

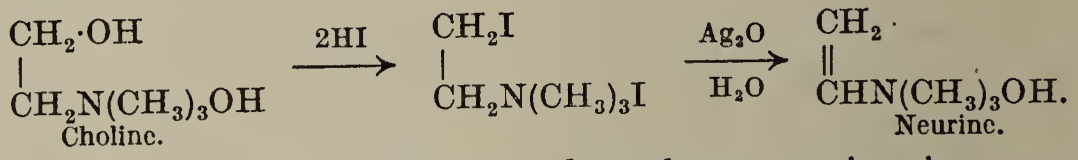
Choline deliquesces in the air. It possesses a strong alkaline reaction and absorbs CO_2. Its platinum double salt, $(C_5H_{14}ONCl)_2{\cdot}PtCl_4$, crystallizes in beautiful reddish-yellow plates, insoluble in alcohol. *Choline derivatives*, see Ber. **27**, R. 738 : Bull. Soc. Chim. [4] **15**, 544.

Acetylcholine has a powerful, though temporary, depressant effect on the blood pressure : it also causes muscular contraction and may be concerned in the regulation of intestinal peristalsis. It has recently been isolated from the spleen (J. physiol. **68**, 97).

iso*Choline*, $CH_3{\cdot}CH(OH){\cdot}NMe_3OH$, is obtained from aldehyde-ammonia (Ber. **16**, 207).

The three *homocholines*, $HO{\cdot}[CH_2]_3{\cdot}NMe_3OH$, $HO{\cdot}CH_2{\cdot}CHMe{\cdot}NMe_3OH$ and $HO{\cdot}CHMe{\cdot}CH_2{\cdot}NMe_3OH$, have been prepared (Ber. **22**, 3321 : Z. physiol. Chem. **67**, 35 : J. Biol. Chem. **10**, 399 : Zeit. Biologie. **57**, 1).

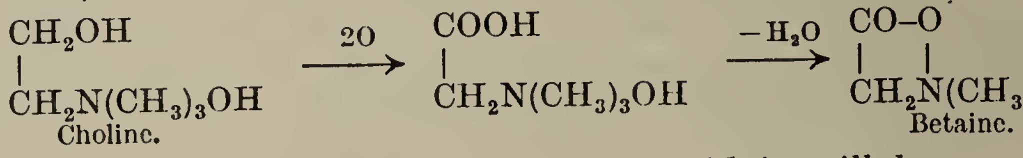
Neurine, *vinyltrimethylammonium hydroxide*, $CH_2 : CH{\cdot}NMe_3OH$, is produced from choline by putrefaction, or by boiling with barium hydroxide solution. It has also been isolated from brain tissue. It occurs among the ptomaines, which are produced by breakdown of protein, particularly in dead animal tissue. It may be obtained from the bromide corresponding with choline (obtained by treating ethylene bromide with trimethylamine), and the iodide (resulting from the action of HI on choline) when they are subjected to the action of moist silver oxide :



$$\begin{array}{c}CH_2{\cdot}OH\\ |\\ CH_2N(CH_3)_3OH\\ \text{Choline.}\end{array} \xrightarrow{2HI} \begin{array}{c}CH_2I\\ |\\ CH_2N(CH_3)_3I\end{array} \xrightarrow[H_2O]{Ag_2O} \begin{array}{c}CH_2\\ \|\\ CHN(CH_3)_3OH.\\ \text{Neurine.}\end{array}$$

Contrary to choline, which is harmless, neurine is exceedingly poisonous.

Betaine, *trimethylglycocoll*, *oxyneurine*, $\begin{array}{l}CO—O\\ |\quad\ \ |\\ CH_2—N(CH_3)_3\end{array}$, is allied to choline and neurine, from which it is obtained by oxidation (*Liebreich*, Ber. **2**, 13) :



$$\begin{array}{c}CH_2OH\\ |\\ CH_2N(CH_3)_3OH\\ \text{Choline.}\end{array} \xrightarrow{2O} \begin{array}{c}COOH\\ |\\ CH_2N(CH_3)_3OH\end{array} \xrightarrow{-H_2O} \begin{array}{c}CO–O\\ |\quad\ |\\ CH_2N(CH_3)_3.\\ \text{Betaine.}\end{array}$$

As it is a derivative of amino-acetic acid it will be more closely examined, in company with other betaines, with the amino-fatty acids.

β-Amino-ethyl ether, $C_2H_5OCH_2CH_2NH_2$, b.p. 108°, is obtained from β-chloro- or β-bromo-ethylamine by means of sodium alcoholate.

β-Dimethylaminoethyl ether, $C_2H_5OCH_2{\cdot}CH_2N(CH_3)_2$, b.p. 121°, occurs in the breakdown products of various morphine bases (Vol. II : Alkaloids) (Ber. **37**, 3504 : **38**, 3150).

Dihydroxydiethylamine, $NH(CH_2CH_2OH)_2$, m.p. 28°, b.p. 270°/100 mm., is prepared from ethylene oxide and dibromodiethylamine.

β-Diaminoethyl ether, $O(CH_2CH_2NH_2)_2$, b.p. 183–184°, is obtained by the break-down of its diphthalyl derivatives, which, in turn, are prepared from diiodo-ethyl ether and 2 molecules of potassium phthalimide (Ber. **38**, 3411).

Diethyleneimine oxide, *morpholine*, $O{<}\begin{array}{c}CH_2{\cdot}CH_2\\ CH_2{\cdot}CH_2\end{array}{>}NH$, is produced when dihydroxyethylamine is heated to 160° with sulphuric acid, and distilled with potassium hydroxide; also, from diiodoethyl ether (p. 370) and toluenesulphonamide (Vol. II), and subsequent decomposition of the toluenesulphomorpholine formed (Ber. **34**, 2606). See Ber. **22**, 2081, for *homologous morpholines.* It was assumed that the same atomic grouping exists in morphine as in morpholine, hence the name.

Trihydroxytriethylamine, $N(CH_2CH_2OH_3)$, b.p. 278°.

Homologous amino alcohols.

α-Amino-β-propanol, $CH_3CH(OH)\cdot CH_2(NH_2)$, b.p. 161°; *α-amino-β-butanol,* $CH_3CH_2CH(OH)CH_2\cdot NH_2$, b.p. 204°, *β-amino-γ-pentanol,* $CH_3CH_2CH(OH)CH(NH_2)CH_3$, b.p. 174°, etc., are prepared by reduction from the corresponding nitro-alcohols; α-amino-β-propanol and β-amino-γ-butanol, $CH_3CH(OH)CH(NH_2)CH_3$, also from the corresponding *iso*nitroso-ketones; α-amino-β-butanol and β-amino-γ-pentanol also from the corresponding amino-ketones (Ber. **32**, 1905: **33**, 3169: **37**, 2480: C. 1902, I. 716, 717).

α-Amino-δ-butanol, $CH_2(OH)\cdot[CH_2]_2CH_2(NH_2)$, b.p. 206°, is produced from γ-cyanopropyl alcohol by sodium and alcohol (Ber. **33**, 3170); *methyl ether* (Ber. **32**, 948).

Diacetone alkamine, $(CH_3)_2C(NH_2)\cdot CH_2CH(OH)CH_3$, b.p. 175°, results on reducing diacetonamine (p. 274) (Ann. **183**, 290: Ber. **30**, 1318).

γ-Amino-βγ-dimethyl-β-butanol (" *Tetramethylhydroxyethylamine* "), $CMe_2OH\cdot CMe_2NH_2$, b.p. 163°, is obtained from tetramethylethylene oxide and ammonia: like pinacone, the corresponding glycol, it yields a *hexahydrate,* m.p. 31° (C. 1908, I. 810).

Homologous hydroxyethylamines, see C. 1908, I. 1257.

For homologous alkamines, see Ber. **14**, 1876, 2406: **15**, 1143: **28**, 3111: **29**, 1420, etc.

(*b*) **Halogen Alkylamines.**—In the free state these bodies are soluble in water and not very stable. They easily change to salts of the cyclic imines, *e.g.* ε-chloroamylamine, $ClCH_2(CH_2)_4NH_2$, yields piperidine hydrochloride, $\overline{CH_2\cdot(CH_2)_4NH}\cdot HCl$. On the transformation of *tert.-β-* and γ-chloroalkylamines into piperazonium bromides, see p. 387.

Formation: (1) The addition of a halogen acid to unsaturated amines, like vinyl- or allylamine, p. 199 (Ber. **21**, 1055: **24**, 2627, 3220: **30**, 1124).

(2) By the action of halogen acids on hydroxyalkylamines.

(2*a*) By mixing the nitriles of the halogen substituted acids with sodium phenolate, reducing and heating with a halogen acid (Ber. **24**, 3221: **25**, 415):

$$Cl\cdot CH_2CH_2CH_2CN + NaOC_6H_5 = C_6H_5O\cdot CH_2CH_2CH_2CN + NaCl$$

$$C_6H_5OCH_2[CH_2]_2CN \xrightarrow{4H} C_6H_5\cdot OCH_2[CH_2]_2CH_2NH_2 \xrightarrow{2HCl} ClCH_2[CH_2]_3NH_2\cdot HCl.$$

(3) From imidochlorides, which result from the action of PCl_5 on the alkylene dibenzoyl diamines (p. 371), by distillation under reduced pressure (Ber. **38**, 2346).

(4) When the halogen alkyl phthalimides are heated with halogen acids (Ber. **21**, 2665: **22**, 2220: **23**, 90), *e.g.*:

$$\underset{\text{Bromoethylphthalimide.}}{C_6H_4(CO)_2N\cdot CH_2\cdot CH_2Br} \xrightarrow[2H_2O]{HBr} \underset{\text{o-Phthalic acid.}}{C_6H_4(COOH)_2} + BrCH_2\cdot CH_2NH_2\cdot HBr.$$

Chloro-, bromo-, iodo-ethylamine, $ICH_2CH_2NH_2$, are known; transformation of bromoethylamine into ethylene imine, see p. 386. *β-Chloroethyldimethylamine,* $ClCH_2CH_2N\cdot(CH_3)_2$, b.p. 110°, is an oil. Its aqueous solution changes on keeping or evaporation into tetramethylpiperazonium chloride (p. 387) (Ber. **37**, 3507).

β-Bromopropylamine, $CH_3CHBrCH_2NH_2$, results as hydrobromide from boiling allyl mustard oil with hydrobromic acid (Ber. **32**, 367). *γ-Chloropropyldimethylamine,* $ClCH_2CH_2CH_2N(CH_3)_2$, b.p. 135° (Ber. **39**, 1420). *γ-Bromopropylamine,* $BrCH_2CH_2CH_2NH_2$.

β-Bromobutylamine, $CH_3CH_2CHBrCH_2NH_2$. *γ-Chlorobutylamine,* $CH_3CHCl\cdot CH_2CH_2NH_2$ (Ber. **28**, 3111). *δ-Chlorobutylamine,* $ClCH_2[CH_2]_2\cdot NH_2$.

ε-Chloroamylamine, $ClCH_2[CH_2]_4NH_2$. *β-Methyl-ε-chloro-*n*-amylamine,* $CH_2Cl[CH_2]_2CH(CH_3)CH_2NH_2$. *β-*n*-Propyl-ε-chloro-*n*-amylamine,* $CH_2Cl[CH_2]_2CH$-

$(C_3H_7)CH_2NH_2$ (Ber. **27**, 3509 : **28**, 1197). The last four compounds readily lose hydrogen chloride and form respectively pyrrolidine, piperidine, β-pipecoline and 3-propylpiperidine.

ζ-Chlorohexylamine, $Cl{\cdot}[CH_2]_6NH_2$, and *η-chloroheptylamine*, $Cl{\cdot}[CH_2]_7NH_2$, are obtained from the alkylene dibenzimidochlorides (Method 3, above) and readily form cyclic bases.

ββ′-Dibromodiethylamine, $(Br{\cdot}CH_2{\cdot}CH_2)_2NH$ (Ber. **30**, 809).

(*c*) **Sulphur Derivatives of the Amino-alcohols.**—*β-Aminoethyl mercaptan*, $CH_2SH{\cdot}CH_2NH_2$, m.p. 100°, is obtained by the action of potassium hydrosulphide on bromoethylphthalimide, and hydrolysis of the product by hydrochloric acid (Ber. **45**, 1643).

The following sulphides have been prepared from bromoethylphthalimide, and converted into their sulphoxides and sulphones.

Methyl β-aminoethyl sulphide (*β-Methylthiolethylamine*) $MeS{\cdot}CH_2{\cdot}CH_2NH_2$, b.p. 147° : and its sulphoxide and sulphone.

Ethyl β-aminoethyl sulphide, $EtS{\cdot}CH_2CH_2NH_2$, b.p. 163°.

ββ′-Diaminodiethyl sulphide, $(NH_2{\cdot}CH_2{\cdot}CH_2{\cdot})S$, b.p. 232° : its sulphone.

Diaminosulphonal, $(NH_2{\cdot}CH_2CH_2SO_2)_2CMe_2$, m.p. 85° (Ber. **22**, 1138 : **24**, 1112, 2132, 3101 : **35**, 1372 : Ann. **386**, 332).

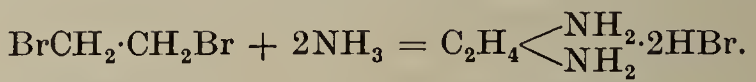
Taurine, $NH_2{\cdot}CH_2CH_2{\cdot}SO_3H$, has already been dealt with (p. 376).

II. Alkylene Diamines.—The divalent alkylene groups can replace two hydrogen atoms in two ammonia molecules, with the production of primary, secondary and tertiary bases. These are di-acid bases, and form salts by direct union with two equivalents of acid. The occurrence of tetramethylenediamine (putrescine) and pentamethylenediamine (cadaverine) among the products of putrefaction of protein (Ptomaines) is of interest. They are formed by simple loss of carbon dioxide from the diamino acids ornithine and lysine.

$$\underset{\text{Lysine.}}{NH_2{\cdot}[CH_2]_4{\cdot}CH(NH_2)COOH} \longrightarrow \underset{\text{Cadaverine.}}{NH_2{\cdot}[CH_2]_5{\cdot}NH_2} + CO_2$$

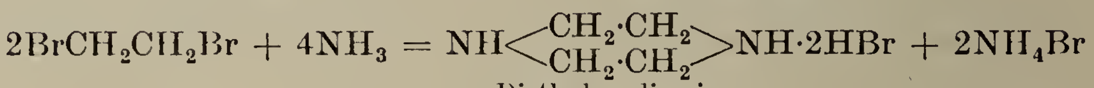
$$\underset{\text{Ornithine.}}{NH_2{\cdot}[CH_2]_3{\cdot}CH(NH_2)COOH} \longrightarrow \underset{\text{Putrescine.}}{NH_2{\cdot}[CH_2]_4{\cdot}NH_2} + CO_2$$

Formation.—(1) They are prepared by heating the alkylene bromides with alcoholic ammonia to 100° (p. 187) in sealed tubes :



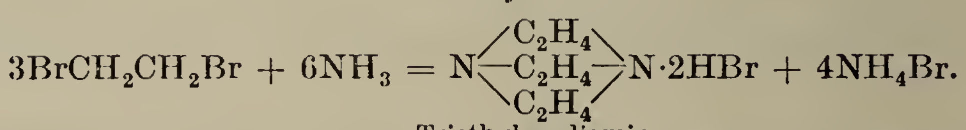
$$BrCH_2{\cdot}CH_2Br + 2NH_3 = C_2H_4{<}\begin{matrix}NH_2\\NH_2\end{matrix}{\cdot}2HBr.$$

Ethylene bromide. Ethylenediamine.



$$2BrCH_2CH_2Br + 4NH_3 = NH{<}\begin{matrix}CH_2{\cdot}CH_2\\CH_2{\cdot}CH_2\end{matrix}{>}NH{\cdot}2HBr + 2NH_4Br$$

Diethylenediamine.

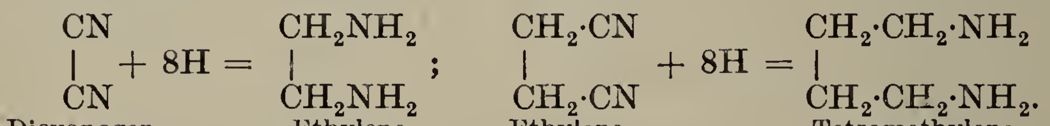


$$3BrCH_2CH_2Br + 6NH_3 = N\begin{matrix}\diagup C_2H_4 \diagdown\\ -C_2H_4- \\ \diagdown C_2H_4 \diagup\end{matrix}N{\cdot}2HBr + 4NH_4Br.$$

Triethylenediamine.

To liberate the diamines, the mixture of their hydrobromides is distilled with KOH and the product is then fractionated.

(2) The reduction of (*a*) alkylene dicyanides or nitriles of dicarboxylic acids (*q.v.*) with metallic sodium and absolute alcohol (see p. 190 and Ber. **20**, 2215) :



$$\begin{matrix}CN\\|\\CN\end{matrix} + 8H = \begin{matrix}CH_2NH_2\\|\\CH_2NH_2\end{matrix} ; \quad \begin{matrix}CH_2{\cdot}CN\\|\\CH_2{\cdot}CN\end{matrix} + 8H = \begin{matrix}CH_2{\cdot}CH_2{\cdot}NH_2\\|\\CH_2{\cdot}CH_2{\cdot}NH_2.\end{matrix}$$

Dicyanogen. Ethylene-diamine. Ethylene-cyanide. Tetramethylene-diamine.

(*b*) By the reduction of the oximes, (*c*) of the hydrazones of the dialdehydes and diketones, and (*d*) of the dinitroparaffins.

In some of these reductions cyclic imines have been observed; thus, in the reduction of ethylene cyanide in the presence of tetramethylene diamine, tetramethylene imine is formed.

(3) From dicarboxylic amides, bromine and alkali hydroxide (Ber. **27,** 511) (p. 191).

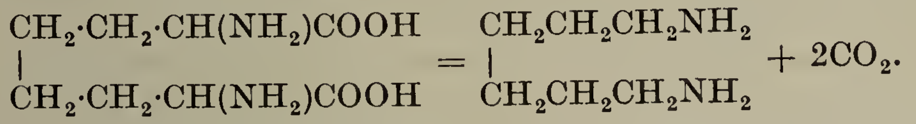
(4) From dicarboxylic azides (J. pr. Chem. [2] **82,** 189).

(5) From alkylene diphthalimides on heating with HCl, or better with KOH:

$$C_6H_4(CO)_2N[CH_2]_3N(CO)_2C_6H_4 \xrightarrow[4H_2O]{2HCl} \begin{array}{l} 2C_6H_4(CO_2H)_2 + \\ HCl{\cdot}NH_2CH_2CH_2CH_2NH_2HCl \end{array}$$

Trimethylenediphthalimide. Trimethylenediaminehydrochloride.

(6) From diamino- mono- and di- carboxylic acids by dry distillation (C. 1905, II. 463):



$$\begin{array}{l} CH_2{\cdot}CH_2{\cdot}CH(NH_2)COOH \\ | \\ CH_2{\cdot}CH_2{\cdot}CH(NH_2)COOH \end{array} = \begin{array}{l} CH_2CH_2CH_2NH_2 \\ | \\ CH_2CH_2CH_2NH_2 \end{array} + 2CO_2.$$

Properties.—The alkylene diamines are liquids or low-melting solids of peculiar odour, which, in the case of those that are volatile, resembles that of ammonia, and recalls that of piperidine. They fume slightly in the air, and absorb carbon dioxide. It is found that the melting points of the homologous series are not regular in their increase, but those of members containing an even number of C atoms are higher than of those containing an uneven number. The boiling points, on the other hand, show a regular increase (J. pr. Chem. [2] **62,** 192; C. 1901, I. 610).

Reactions.—Alcohol and acid radicals can be introduced into the amino-groups of the diamines in the same manner as in the amino-groups of the monoamines (Action of formaldehyde, see Ber. **36,** 35). The production of the dibenzoyl derivatives, *e.g.* $C_2H_4(NHCOC_6H_5)_2$, upon shaking with benzoyl chloride and sodium hydroxide, and the formation of phenylureas, $(CH_2)_n(NH{\cdot}CO{\cdot}NHC_6H_5)_2$, by the action of phenyl*iso*cyanate, is well adapted for the detection of the diamines (Ber. **21,** 2744: C. 1905, I. 274). On the conversion of the alkylene dibenzoyl diamines into chloroalkylamines and alkylene dichlorides, see p. 371. Nitrous acid converts them into glycols, at the same time unsaturated alcohols and unsaturated hydrocarbons arise (Ber. **27,** R. 197).

Further, the diamines unite directly with water, forming very stable hydrates, which only lose water when distilled over potassium hydroxide.

The diamines form well-characterized derivatives with metallic salts, corresponding to the metalammines, in which one molecule of diamine takes the place of two molecules of ammonia (*cf.* Ber. **44,** 3319: **45,** 164).

The diamines show a great tendency to pass over into heterocyclic compounds: thus, cyclic imines are formed by loss of ammonium chloride when their hydrochlorides are distilled:

$$CH_2\left<\begin{array}{l} CH_2{\cdot}CH_2{\cdot}NH_2,\ HCl \\ CH_2{\cdot}CH_2{\cdot}NH_2,\ HCl \end{array}\right. \longrightarrow CH_2\left<\begin{array}{l} CH_2{\cdot}CH_2 \\ CH_2{\cdot}CH_2 \end{array}\right>NH,\ HCl + NH_4Cl.$$

(For other examples of the formation of heterocyclic rings, see under Ethylenediamine.)

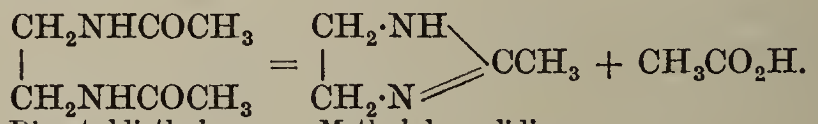
Methylenediamine, $CH_2(NH_2)_2$, is very unstable in the form of the free base. Its salts are obtained by hydrolysis by mineral acids of methylenediformamide, obtained by the condensation of formamide with trioxymethylene (Ber. **47**, 2698).

Ethylenediamine, $C_2H_4{<}\begin{smallmatrix}NH_2\\NH_2\end{smallmatrix}$, m.p. 8·5°, b.p. 116·5°, combines with water to form the *hydrate*, m.p. 10°, and b.p. 118°. It reacts strongly alkaline, and has an ammoniacal odour. Nitrous acid converts it into ethylene oxide.

Ethylenedinitramine, $NO_2NHCH_2{\cdot}CH_2NHNO_2$ (Ber. **22**, R. 295). *Thionylethylenediamine*, $SO : N{\cdot}CH_2{\cdot}CH_2{\cdot}N : SO$, m.p. 5°, b.p. 100°/25 mm. (Ber. **30**, 1009).

Ethylenediamine and $\alpha\beta$-propylenediamine, like the *ortho*-diamines of the benzene series, combine with orthodiketones, *e.g.* phenanthraquinone and benzil, to form pyrazine derivatives, similar in structure to the quinoxalines. They also unite with the benzaldehydes and benzoketones (Ber. **20**, 276 : **21**, 2358). Action on ethylenediamine of $CSCl_2$ (Ber. **27**, 1663), and of aldehydes (C. 1899, I. 594 : Ber. **40**, 881).

Diacetylethylenediamine, m.p. 172°, consists of colourless needles. When this compound is heated beyond its melting point, water splits off, and there follows an inner condensation that leads to the formation of a cyclic base, *methyl gloxalidine*, which under the name *Lysidine*, m.p. 105°, b.p. 223°, has been recommended as a solvent for uric acid (Ber. **28**, 1176). The corresponding propylene, trimethylene and tetramethylene diamine derivatives react similarly (Ber. **36**, 338) :



Diacetyldiethylenediamine. Methylglyoxalidine.

Propylenediamine, $\begin{matrix}CH_3{\cdot}CH{\cdot}NH_2\\ |\\ CH_2{\cdot}NH_2\end{matrix}$, b.p. 119–120° (Ber. **21**, 2359), has been resolved into optically active components by means of *d*-tartaric acid $[\alpha]_D \pm 29{\cdot}7°$ (Ber. **42**, 55).

$\beta\gamma$-Diaminobutane, b.p. 56–60°/55 mm. (hydrate), is obtained by catalytic reduction of dimethylglyoxime (C. 1927, I. 58).

Trimethylenediamine, $NH_2{\cdot}(CH_2)_3{\cdot}NH_2$, b.p. 135–136° (Ber. **17**, 1799 : **21**, 2670), has been prepared by general methods 1, 3, and 4 (from glutaric diazide) and (2*d*) by reduction of $\alpha\gamma$-dinitropropane (p. 186).

$\beta\delta$-Diamino-β-methylpentane, $(CH_3)_2C(NH_2)CH_2CH(NH_2)CH_3$, is obtained from diacetoneamine-oxime (p. 274) by reduction with sodium amalgam (Monatsh. **23**, 9) ; also by reduction of acetyl acetone dioxime with sodium and alcohol. By the second method a *labile* α-diamino compound, b.p. 47°/20 mm., is produced which is converted into the *stable* compound, b.p. 44°/22 mm., by prolonged boiling with alkalis. Both bases yield cyclic ethenyl amidines when heated with acetic acid (see above) (Ber. **32**, 1191).

Tetramethylenediamine, *putrescine*, *$\alpha\delta$-diaminobutane*, $NH_2[CH_2]_4NH_2$, m.p. 27°, is obtained from ethylene cyanide by general methods 2*a* and 2*b* from succinaldehyde dioxime (p. 408) (Ber. **22**, 1970 : **40**, 3872). It is found in the urine and fæces in cases of cystinuria. *Tetramethyltetramethylenediamine*, $(CH_3)_2N{\cdot}[CH_2]_4{\cdot}N(CH_3)_2$, b.p. 169°, occurs in *Hyoscyamus*, Henbane (Ber. **40**, 3869).

Spermine (*NN′-Di-γ-aminopropylputrescine*), $NH_2{\cdot}[CH_2]_3{\cdot}NH{\cdot}[CH_2]_4{\cdot}NH{\cdot}[CH_2]_3{\cdot}NH_2$, was first obtained from fresh human semen by *Schreiner*. It can be obtained synthetically from putrescine and γ-iodopropylphthalimide (Z. physiol. Chem. **163**, 219). It was first synthesized by Dudley, Rosenheim and Starling by condensing putrescine with phenyl γ-bromopropyl ether, replacing the phenoxy groups in the resulting compound with bromine by the action of hydrobromic acid, and then acting on the dibromo-compound with ammonia (Biochem. J. **20**, 1091).

It forms a very characteristic sparingly soluble crystalline phosphate.

Spermidine is a simpler base, $NH_2{\cdot}[CH_2]_3{\cdot}NH{\cdot}[CH_2]_4{\cdot}NH_2$, which accompanies spermine in many tissue extracts (Biochem. J. **21**, 97).

αδ-Diaminopentane, $CH_3 \cdot CH(NH_2) \cdot [CH_2]_3 \cdot NH_2$, b.p. 172°, is obtained by reduction of pyrotartaric nitrile.

αδ-Diamino-β-methylbutane, $NH_2CH_2 \cdot CHMe \cdot CH_2 \cdot CH_2NH_2$, b.p. 173°, is obtained by reduction of pyrotartaric nitrile, or by the action of hypochlorite on β-methyladipic amide (Ber. **28**, 2954 : D.R.P. 216808 : C. 1910, I. 311).

βε-Diaminohexane, $CH_3 \cdot CH(NH_2) \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot CH_3$, b.p. 175°, is formed by reduction of the diphenylhydrazone of acetonylacetone. It exists in two stereoisomeric forms which are characterized by their benzoyl derivatives (*α-Dibenzoyl derivative,* m.p. 238°, *β-,* m.p. 183–185°) (Ber. **28**, 379).

αδ-Diamino-β-methylpentane, $CH_3CH(NH_2)CH_2 \cdot CH(CH_3)CH_2NH_2$, b.p. 175°, is obtained from α-methyl lævulindialdoxime (p. 408) according to method of formation 2*b* (Ber. **23**, 1790).

Pentamethylenediamine, *cadaverine, αε-diaminopentane,* $NH_2CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2CH_2NH_2$, b.p. 178–179°, is obtained by the reduction of trimethylene cyanide (Ber. **18**, 2956 : **19**, 780) ; also from pentamethylene diphthalimide (Preparation, see Ber. **37**, 3583) ; and further, from lysine (αε-diaminocaproic acid) (mode of formation 6, p. 383). It forms a hydrate containing $2H_2O$ (Ber. **27**, R. 580). It occurs as *cadaverine,* a ptomaine isolated from decaying corpses (Ber. **20**, 2216, and R. 69).

Neuridine, $C_5H_{14}N_2$ (Ber. **18**, 86), formed by the decay of fish and meat, is isomeric with pentamethylene diamine.

Hexamethylenediamine, *αζ-diaminohexane,* $NH_2[CH_2]_6NH_2$, m.p. 42°, b.p. 100/°20 mm., is formed in the hydrolysis of hexamethylenediethylurethane, $[CH_2]_6(NHCO_2C_2H_5)_2$, m.p. 84°, which results upon boiling suberic acid azide with alcohol (J. pr. Chem. [2] **62**, 206). Also from αζ-diaminosuberic acid by distillation (mode of formation 6, p. 383) ; further, by reduction and hydrolysis of ε-benzoylaminocaproic acid nitrile, $C_6H_5CONH[CH_2]_5CN$ (Ber. **38**, 2204).

Heptamethylenediamine, $NH_2[CH_2]_7NH_2$, m.p. 29°, b.p. 224°, is prepared from azelaic amide and KBrO, and from pimelic nitrile by reduction (Ber. **38**, 2204).

Octamethylenediamine, *αθ-Diamino-octane,* $NH_2 \cdot [CH_2]_2 \cdot NH_2$, m.p. 51°, b.p. 226°, is obtained from the amide or azide of sebacic acid (method of formation 3 or 4) (J. pr. Chem. [2] **62**, 227) ; and from diaminosebacic acid (method of formation 6, p. 383). Its hydrochloride gives 1-butylpyrrolidine on heating (C. 1906, II. 527).

αι-Diamino-nonane, m.p. 37°, b.p. 258°, is obtained from azelaic nitrile (*q.v.*) (C. 1897, II. 849).

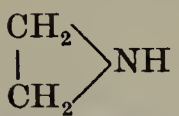
Decamethylenediamine, m.p. 61·5°, b.p. 140°/12 mm., results by reduction of the nitrile of sebacic acid (Ber. **25**, 2253).

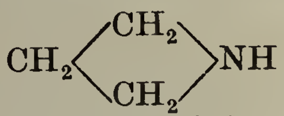
Cyclic Imines

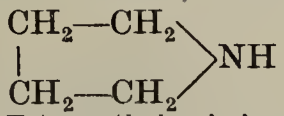
Two classes of these substances are known—the alkylene monimines, which contain one imino-group, and the dialkylene diimines, which contain two alkylene residues and two imino-groups.

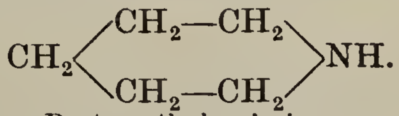
I. Alkylene Monimines.

To this group belong compounds corresponding with the alkylene oxides :

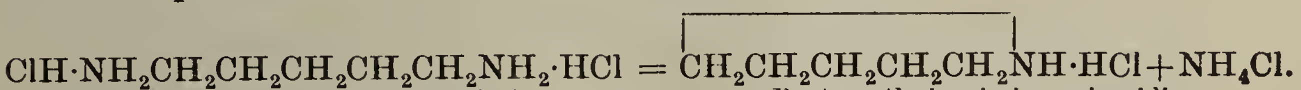

Ethyleneimine.


Trimethyleneimine.


Tetramethyleneimine.

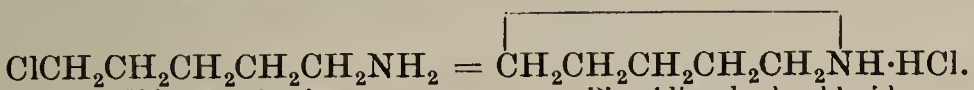

Pentamethyleneimine.

Methods of Formation.—(1) Upon heating the diamine hydrochlorides, when ammonia splits off as ammonium chloride, *e.g.* :


$$ClH \cdot NH_2CH_2CH_2CH_2CH_2CH_2NH_2 \cdot HCl = CH_2CH_2CH_2CH_2CH_2NH \cdot HCl + NH_4Cl.$$

Pentamethylenediamine hydrochloride. Pentamethyleneimine, piperidine.

(2) By the splitting-off of halogen acid from the halogenalkylamines—*e.g.* when the hydrochloride is heated, or when it is digested with dilute potassium hydroxide (Ber. **24**, 3231 : **25**, 415) :


$$ClCH_2CH_2CH_2CH_2CH_2NH_2 = CH_2CH_2CH_2CH_2CH_2NH \cdot HCl.$$

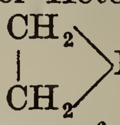
ε-Chloroamylamine. Piperidine hydrochloride.

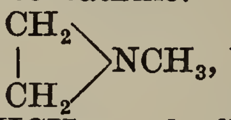
(3) They are produced, together with the diamines, in the reduction of alkylene dicyanides.

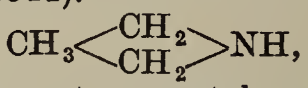
The tendency to ring formation is, as in the case of the ethylene oxides, dependent upon the number of members in the ring. The change of the tetra- and pentamethylenediamines into ring compounds proceeds smoothly, by simply heating their hydrochlorides, whereas trimethylenediamine only yields small amounts of the trimethyleneimine, and ethylenediamine no ethyleneimine at all under these conditions. The rings containing more than seven members are not formed by this method, but alkyl derivatives of pyrrolidine are formed by a process of intramolecular change (Ber. **39**, 4110 : C. 1906, II. 527, 1126).

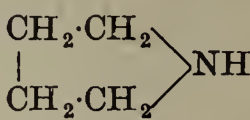
Like the ease of formation, the stability of these ring compounds is also dependent upon the number of members in the ring.

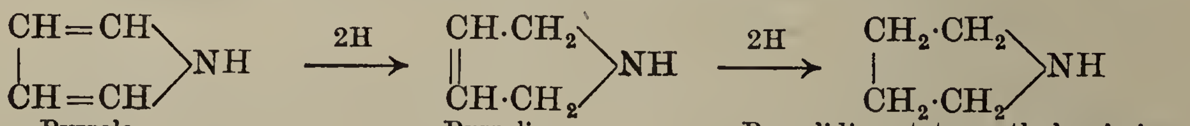
Whilst ethyleneimine is easily decomposed (see below), the tetra- and pentamethyleneimines are very stable, and special methods are required to break them open. Such are : (1) the *exhaustive methylation* method, whereby the quaternary ammonium iodides are decomposed into olefine dialkyl amines by means of alkali (see pp. 115, 199); (2) oxidation of the benzoyl derivatives, which produces benzoylamino-fatty acids ; (3) heating benzoyl derivatives with phosphoric halides, forming dihalogen paraffins and benzonitrile (comp. p. 371). These methods will be discussed under Heterocyclic compounds (Vol. II).

Ethyleneimine, *dimethyleneimine,*  $\left.\begin{array}{l}CH_2\\ |\\ CH_2\end{array}\right>NH$, b.p. 55°, $D_{20} = 0{\cdot}8321$, is obtained from bromoethylamine by means of Ag_2O or potassium hydroxide solution. It is a water-clear liquid, which smells strongly of ammonia, dissolves in water, and acts corrosively on the skin. It is stable against permanganate and bromine, which shows that the above formula is correct rather than the earlier vinyl formula which was assigned to it. With benzenesulphochloride (Vol. II) and alkali, it forms a sulphonamide, insoluble in alkali. It combines with hydrobromic acid in the cold to form bromoethylamine, with H_2S to thiodiethylamine, and with sulphurous acid to taurine.

N-*Methylethyleneimine,*  $\left.\begin{array}{l}CH_2\\ |\\ CH_2\end{array}\right>NCH_3$, b.p. 28°, is prepared from chloroethylmethylamine, $ClCH_2CH_2NHCH_3$, and alkali. Similarly to ethyleneimine, it is converted by iodomethane into iodo-ethyl trimethyl ammonium iodide, $ICH_2{\text -}CH_2N(CH_3)_2I$ (Ber. **34**, 3544).

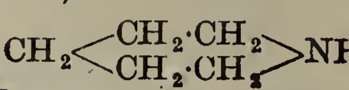
Trimethyleneimine,  $CH_3\left<\begin{array}{l}CH_2\\ CH_2\end{array}\right>NH$, b.p. 63°, $D_{20} = 0{\cdot}8436$. If trimethylene bromide and alkali react on *p*-toluenesulphonamide, *p*-toluenesulphotrimethylene imide is produced ; and when this is hydrolysed by sodium in amyl alcohol solution, trimethyleneimine is produced. It is easily decomposed by acids, as is ethyleneimine (Ber. **32**, 2031).

Tetramethyleneimine, *tetrahydropyrrole, pyrrolidine,*  $\left.\begin{array}{l}CH_2{\cdot}CH_2\\ |\\ CH_2{\cdot}CH_2\end{array}\right>NH$, b.p. 87°, is obtained from tetramethylenediamine (method of formation 1) ; from δ-chlorobutylamine and potassium hydroxide (method 2) (Ber. **24**, 3231), and by the reduction of pyrroline, the first reduction-product of pyrrole (Ber. **18**, 2079), and of succinimide (see Succinic acid) (Ber. **32**, 951) :

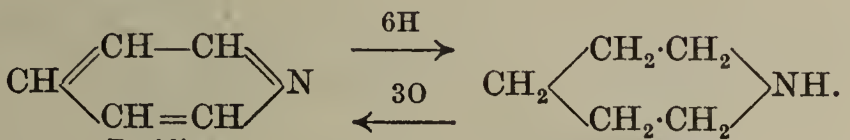


Pyrrole. Pyrroline. Pyrrolidine, tetramethyleneimine.

Pyrrolidine has an odour resembling that of piperidine. *Tetramethylenenitrosamine,* C_4H_8NNO, b.p. 214° (Ber. **21**, 290). N-*Methylpyrrolidine,* $(CH_2)_4{\text -}NCH_3$, b.p. 82°, is produced by bromination of methyl-*n*-butylamine, followed by splitting off of HBr by conc. H_2So_4 (Ber. **42**, 3427 : **43**, 2035).

Pentamethyleneimine, *piperidine, hexahydropyridine,*  $CH_2\left<\begin{array}{l}CH_2{\cdot}CH_2\\ CH_2{\cdot}CH_2\end{array}\right>NH$, b.p. 106°, is obtained according to methods **1**, **2** (Ber. **25**, 415) and **3** (p. 385) ;

also from piperine (Vol. III), and by the reduction of pyridine, into which it passes when it is oxidized :



Pyridine. Piperidine.

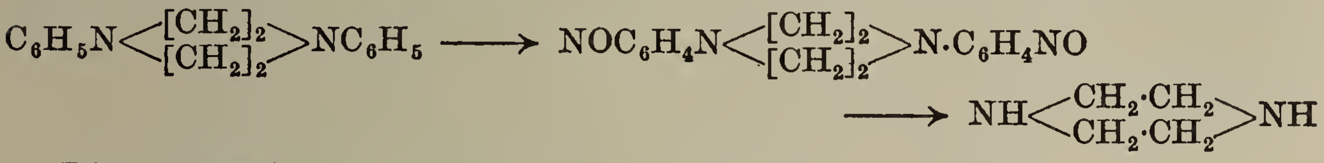
Piperidine bears the same relation to pyridine as pyrrolidine to pyrrole. Tetramethyleneimine and pentamethyleneimine link the pyrrole and pyridine groups to the simple aliphatic substances.

The pyrrole and pyridine derivatives will be discussed later in connection with the heterocyclic ring systems, together with allied bodies, and pyrrolidine and piperidine will again be referred to.

Hexamethyleneimine, $\begin{matrix}CH_2\cdot CH_2\cdot CH_2\\ |\\ CH_2\cdot CH_2\cdot CH_2\end{matrix}>NH$, is formed together with complex products, in small quantity, by the action of alkali on ζ-bromohexylamine (Ber. **43**, 2853).

II. **Dialkylenediimines.**

Diethylenediimine, *piperazine, hexahydropyrazine,* $NH<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>NH$, m.p. 104°, b.p. 145°, was first prepared by the action of ammonia on ethylene chloride. It is produced by heating ethylenediamine hydrochloride (Ber. **21**, 758), and by the reduction of pyrazine, $N\leqslant\begin{matrix}CH=CH\\CH-CH\end{matrix}\geqslant N$ (Ber. **26**, 724). It is technically made from diphenyl diethylenediimine, the reaction-product of aniline and ethylene bromide, when it is converted into the *p*-dinitroso-compound, and the latter then broken down into *p*-dinitrosophenol and diethylenediimine :



$$C_6H_5N<\begin{matrix}[CH_2]_2\\[CH_2]_2\end{matrix}>NC_6H_5 \longrightarrow NOC_6H_4N<\begin{matrix}[CH_2]_2\\[CH_2]_2\end{matrix}>N\cdot C_6H_4NO \longrightarrow NH<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>NH$$

Diethylenediimine, or piperazine, is a strong base, soluble in water, which, upon distillation with zinc dust, changes to pyrazine (Vol. III) (Ber. **26**, R. 441).

The compound 2 : **5-diketopiperazine,** $HN<\begin{matrix}CH_2\cdot CO\\CO\cdot CH_2\end{matrix}>NH$, and its derivatives are of great importance, as they are readily formed from α-amino acids (see p. 446) and may play a part in the structure of protein molecules.

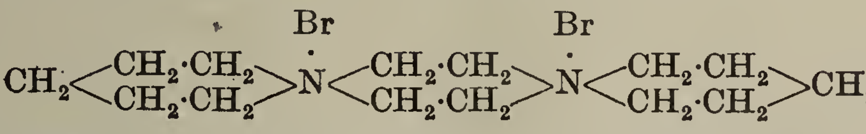
Quaternary piperazonium halides are obtained by the action of iodo-alkyls on piperazine (Ber. **36**, 145) ; and also by spontaneous change of β-chloro- or bromoethyl dialkylamines (p. 381) whereby the oily bases are converted into solid neutral salts :

$$2ClCH_2CH_2N(CH_3)_2 \longrightarrow ClN(CH_3)_2<\begin{matrix}CH_2-CH_2\\CH_2-CH_2\end{matrix}>N(CH_3)_2Cl.$$

Chloroethyldimethylamine. Tetramethylpiperazonium dichloride.

The secondary base β-Chloroethylmethylamine yields ethylenemethylimine and the polymeric *NN*-dimethylpiperazine when acted on by alkali, whereas the primary bases chloro- and bromoethylamine yield only ethyleneimine.

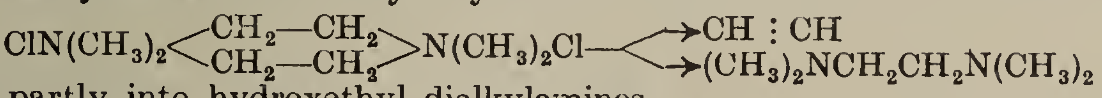
Piperidine*spiro***piperazine***spiro***piperidine dibromide,**



$$CH_2<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>\overset{Br}{\dot{N}}<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>\overset{Br}{\dot{N}}<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>CH_2,$$

is obtained, analogously to the above, from β-bromoethylpiperidine, $(CH_2)_5NCH_2$-CH_2Br. It is also prepared from piperazine and two molecules of dibromopentane.

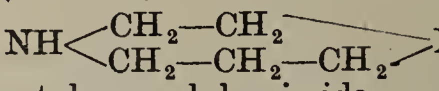
These quaternary piperazonium halides are decomposed by alkalis partly into acetylene and tetraalkylethylenediamines :

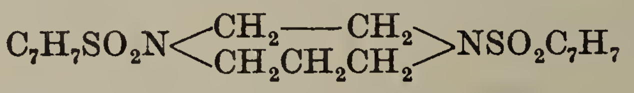


$$ClN(CH_3)_2<\begin{matrix}CH_2-CH_2\\CH_2-CH_2\end{matrix}>N(CH_3)_2Cl-<\begin{matrix}\rightarrow CH:CH\\ \rightarrow (CH_3)_2NCH_2CH_2N(CH_3)_2\end{matrix}$$

and partly into hydroxethyl dialkylamines.

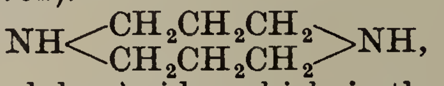
Dry distillation decomposes tetramethylpiperazonium chloride into chloromethane and *N*-dimethylpiperazine (Ber. **37**, 3507 : **38**, 3136 : **40**, 2936).

Trimethyleneethylenediimine,  $NH<\begin{matrix}CH_2—CH_2\text{———} \\ CH_2—CH_2—CH_2\end{matrix}>NH$, b.p. 169°, is prepared from trimethyleneethylene-*p*-toluenesulphonimide,



$$C_7H_7SO_2N<\begin{matrix}CH_2\text{——}CH_2 \\ CH_2CH_2CH_2\end{matrix}>NSO_2C_7H_7$$

and HCl (Ber. **32**, 2041 : **33**, 761).

Bis-trimethylenediimine,  $NH<\begin{matrix}CH_2CH_2CH_2 \\ CH_2CH_2CH_2\end{matrix}>NH$, m.p. 15°, b.p. 187°, is obtained from its *p*-toluene sulphonimide, which is the product of reaction between trimethylene bromide and the di-sodium salt of di-*p*-toluenesulphotrimethylene diamide, $CH_3C_6H_4SO_2NNa{\cdot}CH_2CH_2CH_2{\cdot}NNaSO_2C_6H_4CH_3$ (Ber. **32**, 2038).

The spontaneous change of γ-chloropropyldimethylamine, $ClCH_2CH_2CH_2N(CH_3)_2$, produces bis-trimethylenetetramethyldiimonium chloride, $Cl(CH_3)_2N[CH_2CH_2CH_2]_2N(CH_3)_2Cl$ (comp. above, piperazonium bromide ; and Ber. **39**, 1420).

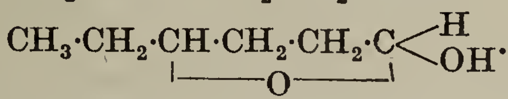
HYDROXYALDEHYDES AND HYDROXYKETONES

2. HYDROXYALDEHYDES. ALDEHYDE-ALCOHOLS

These contain both an alcoholic hydroxyl group and the aldehyde group CHO, hence their properties are both those of alcohols and aldehydes (p. 229). The addition of 2 H-atoms changes them to glycols, whilst by oxidation they yield the hydroxy acids, containing a like number of carbon atoms. The most important representatives of this group are the β-hydroxyaldehydes or *aldols*, which result from the aldol condensation of the simple aldehydes.

The hydroxyaldehydes are of importance theoretically as they form simple models of the important polyhydroxyaldehydes, the monosaccharides. The simple hydroxyaldehydes can react both in the normal open chain form, and also in a cyclic form corresponding to the cyclic forms of the sugars suggested by Tollens. Thus they form semi-acetals or " glucosides " with alcoholic hydrogen chloride instead of the normal acetals formed by the non-hydroxylated aldehydes:

e.g. Open chain form $CH_3{\cdot}CH_2{\cdot}CHOH{\cdot}CH_2{\cdot}CH_2{\cdot}CHO$.

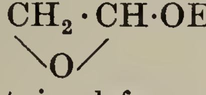
Butylene oxide form  $CH_3{\cdot}CH_2{\cdot}\underbrace{CH{\cdot}CH_2{\cdot}CH_2{\cdot}C}_{O}{<}^{H}_{OH}$.

These relationships exist among the α-hydroxyaldehydes (Ber. **54**, 2150) as well as among the γ- and δ-compounds.

Glycollic aldehyde, [ethanolal], $CH_2(OH)CHO$, m.p. 95–98°, is the first aldehyde of glycol, and can be obtained from it by oxidation with hydrogen peroxide in the presence of ferrous salts. It is also prepared from bromoacetaldehyde and barium hydroxide solution, and from chloroacetal by treatment with alkali followed by acid (C. 1903, I. 1427). Further, it is very easily produced from dihydroxymaleic acid (an oxidation product of tartaric acid) by heating it with water at 50–60°. It is formed in small quantities by condensation of formaldehyde by means of $CaCO_3$ (Ber. **39**, 50). Glycollic aldehyde remains behind, when its solution evaporates, as a slightly sweet syrup; this can be distilled under reduced pressure, when it solidifies; on melting it undergoes condensation very easily. Bromine water oxidizes it to glycollic acid (p. 414), whilst it is condensed by sodium hydroxide solution to *tetrose* (*q.v.*), and by sodium carbonate solution to *acrose* (*q.v.*) (Ber. **25**, 2552, 2984: C. 1899, II. 88: 1900, I. 285). Hydroxylamine gives rise to an oily *oxime* (C. 1900, II. 312), and phenylhydrazine and acetic acid produce *glyoxalosazone* (p. 409).

The following derivatives have already been discussed: the monohalogenacetaldehydes (p. 240) and their acetals (p. 242) and dichloroethyl alcohol (p. 144).

The *diethylacetal*, $CH_2OH{\cdot}CH(O{\cdot}C_2H_5)_2$, b.p. 167°, is obtained from bromoacetal (Ber. **5**, 10). The *dimethylacetal*, $CH_2OH{\cdot}CH(OMe)_2$, b.p. 158°, is obtained from glycollic aldehyde and methyl alcoholic hydrogen chloride (Ber. **39**, 3053).

The *ethyl semiacetal*,  $\underbrace{CH_2{\cdot}CH}_{O}{\cdot}OEt$, b.p. 90°/12 mm., is a derivative of the " cyclo-form " and is obtained from vinyl ethyl ether and perbenzoic acid. It is the simplest glucoside model (Ber. **54**, 2150).

Ethoxyacetaldehyde, $EtO{\cdot}CH_2{\cdot}CHO$, b.p. 71–73°, is obtained from its acetal by the action of very dilute sulphuric acid, or of one mol. of water in acetone solution. The *acetal*, $EtO{\cdot}CH_2{\cdot}CH(OEt)_2$, b.p. 168°, is obtained from αβ-dichloroethyl ether or chloro- or bromoacetal and sodium ethoxide (Ber. **39**, 2644 : C. 1905, I. 1219 : 1907, I. 706).

Phenoxyacetal, $C_6H_5O{\cdot}CH_2{\cdot}CH(OEt)_2$, b.p. 257° (Ber. **28**, R. 295).

Lactic aldehyde, *α-hydroxypropionic aldehyde*, $CH_3{\cdot}CH(OH){\cdot}CHO$, is prepared from the acetal of methylglyoxal, $CH_3{\cdot}CO{\cdot}CH(OEt)_2$ (p. 400), by reduction, followed by hydrolysis of the lactaldehyde *acetal*, $CH_3{\cdot}CH(OH){\cdot}CH(OEt)_2$, b.p. 169°, with cold dilute sulphuric acid. The lactaldehyde thus obtained (m.p. 105°) is like glycollaldehyde bimolecular, but gradually changes into the monomolecular form in aqueous solution. It very readily undergoes isomeric change into hydroxyacetone, this change occurring when lactaldehyde is distilled at the ordinary pressure. Hydroxyacetone is also obtained instead of the expected lactaldehyde when *α-acetoxypropionaldehyde*, $CH_3{\cdot}CH(OAc){\cdot}CHO$, b.p. 52–55°/15 mm. (from α-iodopropionaldehyde and silver acetate), is heated with water, or when α-bromopropionaldehyde is heated with potassium formate and methyl alcohol (Ann. **335**, 266 : Ber. **41**, 3599, 3612). *Dichloro*iso*propyl alcohol*, $Cl_2CHCH(OH)CH_3$, b.p. 147°, can be looked on as a derivative of α-hydroxypropionaldehyde. It is prepared from dichloroaldehyde and CH_3MgBr (Ber. **40**, 27).

α-Hydroxy*iso*butyraldehyde, $(CH_3)_2C(OH){\cdot}CHO$, b.p. 137°, is prepared from *α-bromo*iso*butyraldehyde*, b.p. 113°, and water. It is an easily polymerizable liquid. Sodium hydroxide solution converts it into *iso*butylene glycol (p. **363**) and α-hydroxy*iso*butyric acid (Monatsh. **21**, 1122).

β-Hydroxypropionaldehyde, *hydracrylic aldehyde*, $HOCH_2{\cdot}CH_2CHO$, b.p. 90°/18 mm., is produced when acrolein is heated with water to 100° : *semicarbazone*, m.p. 114°, regenerates acrolein when treated with bisulphate. It easily polymerizes. Alkali partially converts it to crotonaldehyde (Ann. **335**, 219). *β-Hydroxypropionacetal*, $OHCH_2{\cdot}CH_2{\cdot}CH(OC_2H_5)_2$, b.p. 98°/20 mm., is prepared by prolonged boiling of dilute sodium hydroxide solution at 115° with β-chloropropionacetal, b.p. 74°/20 mm., the addition product of acrolein acetal (p. 254) and HCl (Ber. **33**, 2760).

Aldol, *β-hydroxybutyraldehyde*, $CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}CHO$, b.p. 77°/16 mm., $D_0 = 1{\cdot}120$, was discovered by *Wurtz* in 1872. It is obtained by the condensation of acetaldehyde by means of dilute cold hydrochloric acid, and other condensation agents, *e.g.* K_2CO_3 (Ber. **14**, 2069 : **24**, R. 89 : **25**, R. 732 : Monatsh. **22**, 59 : C. 1907, I. 1400).

Aldol freshly prepared is a colourless, odourless liquid, and is miscible with water. It distils under atmospheric pressure, partially reforming acetaldehyde, but it mainly becomes converted into crotonaldehyde and water.

As an aldehyde it will reduce an ammoniacal silver nitrate solution. Heated with silver oxide and water it yields β-hydroxybutyric acid, $CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}CO_2H$.

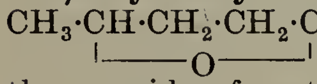
After prolonged standing aldol polymerizes, becoming viscous, sometimes depositing crystals of *paraldol*, $(C_4H_8O_2)_2$, m.p. 80–90° (Monatsh. **21**, 80). If, during the preparation of aldol, the mixture of aldehyde and hydrochloric acid be left undisturbed, the aldol condenses with loss of water to *dialdan*, $C_8H_{14}O_3$, m.p. 139°, a crystalline body which reduces ammoniacal silver solution. *Tetraldan*, $C_{16}H_{28}O_6$, is formed simultaneous with dialdan, and does not reduce silver from its ammoniacal solution (C. 1900, II. 838). *Diethylacetal* of *β-ethoxybutyric aldehyde*, $CH_3{\cdot}CH(OC_2H_5)CH_2{\cdot}CH(OC_2H_5)_2$, b.p. 73°/14 mm. (Ber. **31**, 1014).

The **aldol condensation** is characteristic for this class of substance and occurs among the higher members of the series when a free hydrogen atom exists next to the aldehyde group. Thus, a series of β-hydroxyaldehydes or *aldols* can be prepared. A mixture of two aldehydes yields *mixed aldols*. The condensing agent mostly employed is potassium carbonate :

$$2CH_3{\cdot}CH_2CHO = CH_3CH_2CH(OH)CH(CH_3)CHO$$
$$CH_2O + (CH_3)_2CHCHO = CH_2(OH)C(CH_3)_2CHO.$$

Like aldol itself, the homologous aldols are easily converted into α, β-olefine aldehydes when a hydrogen atom in the α-position is free, and are stable bodies. If, however, there is no α-hydrogen atom present, some members decompose more easily than aldol into the simple aldehyde. Aldols from *iso*butyric aldehyde are further acted on by hot alkali during reaction and are transformed into the corresponding glycols and *iso*butyric acid (p. 359) (*Lieben*, Monatsh. **22**, 289).

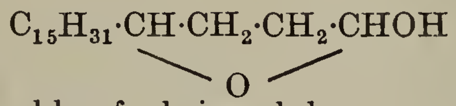
Formisobutyric aldol, $CH_2(OH)\cdot C(CH_3)_2\cdot CHO$, m.p. 90°, b.p. 85°/15 mm., is converted into *β*-dimethyl trimethylene glycol (p. 364) and α-dimethyl *β*-hydroxypropionic acid by the action of alkalis. *Acetopropionic aldol*, $CH_3\cdot CH(OH)\cdot CH(CH_3)CHO$, b.p. 92°/20 mm. *Propionic aldol*, b.p. 95°/23 mm. iso*Butyric aldol*, b.p. 104°–109°/17 mm. iso*Butyric* iso*valeric aldol* is decomposed by heat into its component parts. For other aldols, see C. 1904, I. 199 : II. 1599 ; vapour pressure of the aldols, see Monatsh. **21**, 80.

γ-Hydroxyvaleraldehyde exists practically entirely in the *cyclo*-form,  $\underbrace{CH_3\cdot CH\cdot CH_2\cdot CH_2\cdot CHOH}_{O}$, b.p. 64°/10 mm., and is obtained by breakdown of the ozonide of methylheptenol (Ber. **52**, 1123). The *methyl semiacetal* boils at 116–118°/755 mm. Derivatives of the open chain aldehyde form have been obtained by other methods and are totally different from the derivatives of the *cyclo*-form (Ber. **52**, 1800).

γ-Hydroxycapraldehyde, b.p. 77–80°/11 mm., obtained from allylacetic acid, also exists in the cyclic form, as is shown by its molecular refraction, formation of semiacetals and slow reddening of fuchsin sulphurous acid. *Methyl semiacetal*, b.p. 139–145°/760 mm.

δ-Hydroxycapraldehyde, b.p. 71–78°/11 mm., also exists in the cyclic form, but gradually passes into the open chain form in various reactions. Preparation, see Ber. **55**, 702. *Methyl semiacetal*, b.p. 72–76°/110 mm.

γ-Hydroxynonadecaldehyde (Synthesis, Ber. **56**, 2088) has been isolated in the two forms :

$C_{15}H_{31}\cdot CHOH\cdot CH_2\cdot CH_2\cdot CHO$, m.p. <40° ;  $\underbrace{C_{15}H_{31}\cdot CH\cdot CH_2\cdot CH_2\cdot CHOH}_{O}$ (Cyclic form), m.p. 64°. The cyclic form does not redden fuchsin sulphurous acid even on long standing.

NITROGEN DERIVATIVES OF THE HYDROXYALDEHYDES

Nitroaldehydes.—Nitroacetaldehyde itself is unknown. Its *diethylacetal* $NO_2\cdot CH_2\cdot CH(OEt)_2$, b.p. 90°/14 mm., has been obtained not quite pure by the interaction of silver nitrite and iodoacetal (Ber. **42**, 4044). The *oxime* of nitroacetaldehyde is the so-called methazonic acid, $NO_2\cdot CH_2\cdot CH : NOH$, which is formed by the condensation of two molecules of nitromethane under the action of alkali, with loss of a molecule of water. Concentrated sulphuric acid converts methazonic acid into *iso*cyanilic acid (Ann. **444**, 15 : see p. 294). By the action of thionyl chloride on its ethereal solution, methazonic acid is converted into nitroacetonitrile, and by heating with alkali, it is converted into nitroacetic acid (J. pr. Chem. [2], **81**, 135 : **83**, 453). Phenylhydrazine and aniline produce respectively the *phenylhydrazone*, $NO_2\cdot CH_2\cdot CH : N\cdot NHC_6H_5$, m.p. 74°, and *anil*, $NO_2\cdot CH_2\cdot CH : NC_6H_5$, m.p. 95°, of nitroacetaldehyde (Ber. **40**, 3435).

It is justifiable, on systematic grounds, to include in this section the aldol-like condensation products of aldehydes with potassium dinitromethane (p. 185) :

$$CH_2O + \underset{aci\text{-Dinitromethane.}}{CH(NO_2) : NOOH} \rightleftarrows \underset{aci\text{-Dinitro-ethyl alcohol.}}{CH_2(OH)\cdot C(NO_2) : NO_2H.}$$

The resulting potassium salts form yellow crystals, which, as such or in aqueous solution, decompose into their components on being heated. The free acids are strongly acid, easily decomposable oils. Similar condensation products, *e.g.* *αα-dinitro-alkylamines*, are also obtained from the aldehyde-ammonias or amino-compounds and dinitromethane :

$$CH_3CH(NH_2)OH + CH_2(NO_2)_2 \longrightarrow \underset{\alpha\alpha\text{-Dinitro-}\beta\text{-aminopropane.}}{CH_3\cdot CH(NH_2)CH(NO_2)_2}$$

$$(CH_3)_2NCH_2OH + CH_2(NO_2)_2 \longrightarrow \underset{\alpha\alpha\text{-Dinitro-}\beta\text{-dimethylaminoethane.}}{(CH_3)_2N\cdot CH_2\cdot CH(NO_2)_2.}$$

These bodies are more stable, probably on account of their forming cyclic internal salts (comp. p. 380) between the acid nitro- and the amino-groups

(Ber. **38**, 2031, 2040). Finally, formaldehyde and acetaldehyde unite with nitrobromomethane (p. 182) to form, respectively, *α-nitrobromoethyl alcohol*, $NO_2\cdot CHBr\cdot CH_2OH$, b.p. 147°/45 mm., and *α-nitro-bromo*iso*propyl alcohol*, $NO_2\cdot CHBr\cdot CH(OH)CH_3$, b.p. 149°/42 mm. (C. 1899, I. 179).

Aldehyde-Ammonias.—Ammonia gas converts aldol in ethereal solution into aldol-ammonia, $C_4H_8O_2\cdot NH_3$, a thick syrup, soluble in water. When heated with ammonia the bases, $C_8H_{15}NO_2$, $C_8H_{13}NO$, oxytetraldine (p. 254), and collidine, $C_5H_2N(CH_3)_3$, are formed. With aniline aldol forms methylquinoline. (*Cf.* alkylideneanilines: Vol. III.)

Aminoaldehydes: Aminoacetaldehyde, [ethanalamine], $NH_2\cdot CH_2CHO$, is obtained as a deliquescent hydrochloride when *aminoacetal*, $NH_2\cdot CH_2(OC_2H_5)_2$, b.p. 163°, is treated with cold, concentrated hydrochloric acid. Aminoacetal is produced together with *diacetalylamine*, $NH[CH_2\cdot CH(OEt)_2]_2$, and *triacetalylamine*, $N[CH_2\cdot CH(OEt)_2]_3$, when chloroacetal is treated with ammonia (Ber. **25**, 2355: **27**, 3093: Ann. **363**, 169). Aminoacetaldehyde is also obtained from allylamine by the splitting action of ozone (comp. p. 106, etc.) (Ber. **37**, 612):

$$CH_2:CH\cdot CH_2NH_2 \xrightarrow{O_3} CH_2O + OCH\cdot CH_2\cdot NH_2.$$

By oxidation with mercuric chloride, aminoacetaldehyde yields pyrazine, $N{<}\begin{matrix}CH{-}CH\\CH{=}CH\end{matrix}{>}N$ (Ber. **26**, 1830, 2207).

Alkylaminoacetals, see C. 1908, II. 229. *Dialkylaminoacetals, dialkylaminoacetaldehydes*, and *trialkylammonium salts*, see Ber. **30**, 1504.

Hydrazinoacetaldehyde, Ber. **27**, 2203. *Azidoacetaldehyde*, $N_3CH_2\cdot CHO$, J.C.S. **93**, 1865.

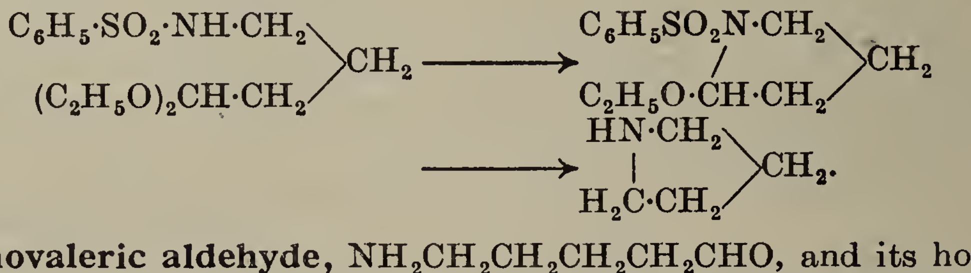
Betaine aldehyde, $(CH_3)_3\overline{N\cdot CH_2CHO}(OH)$ (?) (Ber. **27**, 165), is different from *muscarine*, p. 379), which occurs in fly agaric (*Agaricus muscarius*).

iso*Muscarine*, $HO\cdot CH_2CH(OH)N(CH_3)_3OH$ (?), is obtained from the addition-product of HClO and neurine (p. 380) with silver oxide (Ann. **267**, 532, 291).

α-Aminopropionaldehyde, $CH_3CH(NH_2)CHO$, is obtained by the action of ozone on α-styryl ethylamine (Ber. **37**, 615). *d-α-Aminopropionaldehyde acetal*, $CH_3\cdot CHNH_2\cdot CH(OEt)$, b.p. 55°/11 mm., is obtained by reduction of *d*-alanine ester by sodium amalgam (Ann. **365**, 7).

β-Aminopropionaldehyde, $NH_2CH_2\cdot CH_2\cdot CHO$, is obtained as a salt by the breaking down of its *acetal*, $NH_2CH_2\cdot CH_2CH(OC_2H_5)_2$, b.p. 80°/18 mm., which, in turn, is produced from β-chloropropionic acetal (p. 240), by digestion with alcoholic ammonia. At the same time there is formed iminodipropionic acetal, $HN[CH_2CH_2CH(OC_2H_5)_2]_2$, b.p. 157°/15 mm., which on hydrolysis yields iminodipropionic aldehyde, a substance which undergoes ring-condensation to form β-tetrahydropyridinealdehyde (Ber. **38**, 4162) (Vol. III):

γ-Aminobutyric acetal, $NH_2\cdot CH_2CH_2\cdot CH_2CH(OC_2H_5)_2$, b.p. 196°, results from the reduction of β-cyanopropionic acetal by sodium and alcohol. Its *benzenesulphonyl* derivative condenses spontaneously forming N-*benzenesulpho-α-ethoxypyrrolidine*, which is reduced to pyrrolidine by sodium and amyl alcohol (Ber. **38**, 4157):



δ-Aminovaleric aldehyde, $NH_2CH_2CH_2CH_2CH_2CHO$, and its homologues were thought to have been produced by the oxidation of piperidine (p. 386 and Vol. III) with H_2O_2; but this is now known to yield piperidine oxide, $CH_2{<}\begin{matrix}CH_2{-}CH_2\\CH_2{-}CH_2\end{matrix}{>}N{<}\begin{matrix}H\\O\end{matrix}$ (Ber. **31**, 2687).

3. KETONE-ALCOHOLS OR KETOLS

The ketone alcohols or ketols are distinguished, according to the position of the alcohol or ketone groups, as α- or 1 : 2-, β- or 1 : 3-, γ- or 1 : 4-ketols, etc. The position of these two groups, with reference to each other, influences the chemical character of these bodies more than the type of alcohol group (whether primary, secondary, or tertiary). These alcohols show simultaneously the character of alcohols and of ketones. Like the hydroxyaldehydes (p. 389) the hydroxyketones exist in cyclic forms as well as the normal open chain forms.

A. SATURATED KETOLS

α- or 1 : 2-Ketols

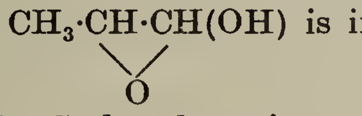
These are characterized by their ready oxidizability ; they reduce Fehling's solution and ammoniacal silver solutions. The 1 : 2 ketols react with phenylhydrazine to produce osazones (diphenylhydrazones of 1 : 2-ketoaldehydes or diketones), the hydroxy group being oxidized to a ketonic group by excess of phenylhydrazine (*cf.* Hexoses).

Hydroxyacetone, *acetylcarbinol, acetone alcohol, pyruvic alcohol,* $CH_3·CO·CH_2OH$, b.p. 145–146°, b.p. 54°/18 mm., is produced by the following reactions :

(1) From chloro- or bromoacetone, best by heating them with potassium formate and methyl alcohol, when the first-formed acetol formate is alcoholysed by the methyl alcohol.

(2) Hydroxyacetone is formed instead of the expected lactaldehyde when α-bromopropionaldehyde is treated with potassium formate and methyl alcohol, or when α-acetoxypropionaldehyde is hydrolysed. It is also obtained when lactaldehyde is distilled under atmospheric pressure. These changes can be represented by the following scheme :

$$CH_3·CHOH·CHO \longrightarrow CH_3·C(OH) : CH(OH) \longrightarrow CH_3·CO·CH_2OH ;$$

it is possible that the cyclic form  $\underbrace{CH_3·CH·CH(OH)}_{O}$ is involved.

(3) From propylene glycol and the *Sorbose bacterium,* or by careful oxidation with bromine water (C. 1899, II. 475 : 1900, I. 280).

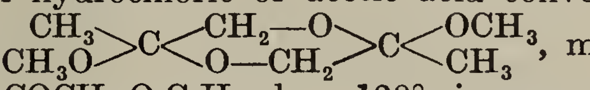
(4) If glycerol vapour is passed over pumice-stone at 430–450° some acetol is formed.

(5) When sucrose or dextrose is fused with potassium hydroxide, acetol results (Ber. **16**, 834).

Acetol reacts acid (C. 1905, II. 29). Reduction with aluminium amalgam yields propylene glycol (p. 363) and acetone (C. 1903, I. 132). Acetol shows a strong reducing action : aqueous copper acetate oxidizes it normally to pyruvic aldehyde, $CH_3·CO·CHO$ (Am. Chem. J. **38**, 583), but when oxidized by the oxides of Cu, Hg, Fe, it is converted into lactic acid, with the probable intermediate formation of pyruvic aldehyde :

$$CH_3CO·CH_2OH \xrightarrow{O} [CH_3CO·CHO] \xrightarrow{H_2O} CH_3CH(OH)COOH.$$

Permanganate, chromic acid, and the like, oxidize acetol into acetic and formic acids (C. 1905, I. 19).

Methyl alcohol containing a trace of hydrochloric or acetic acid converts acetol into bis-acetol methyl alcoholate,  $\begin{smallmatrix}CH_3\\CH_3O\end{smallmatrix}>C<\begin{smallmatrix}CH_2—O\\O—CH_2\end{smallmatrix}>C<\begin{smallmatrix}OCH_3\\CH_3\end{smallmatrix}$, m.p. 130°, b.p. 196°. *Acetol ethyl ether,* $CH_3COCH_2·O·C_2H_5$, b.p. 128°, is prepared from propargyl ethyl ether (p. 158), or synthetically, from ethoxyacetonitrile, $C_2H_5OCH_2CN$, and methyl magnesium iodide. Similar *homologous ethoxymethyl alkyl ketones* (C. 1907, I. 872) may be obtained. On the formation of such ketones from halogen acetoacetic esters, see Ber. **21**, 2648. *Acetol formate,* $HCOO·CH_2COCH_3$, b.p. 169°, and higher esters, see C. 1905, II. 754. Chloro-, bromo-, iodo-acetone (p. 265) are the haloid esters of acetyl carbinol.

Propionyl carbinol, *ethyl ketol, butan-α-ol-β-one,* $CH_3CH_2CO{\cdot}CH_2OH$, b.p. 160°, is obtained from chloromethyl ethyl ketone, $ClCH_2COCH_2CH_3$; also from tetrinic acid (*q.v.*) by the loss of CO_2 on boiling with water. It is oxidized by Fehling's solution to α-hydroxybutyric acid (C. 1905, II. 116).

The *secondary* and *tertiary ketone alcohols* are obtained by the following reactions :

(1) By the reduction of α-diketones.

(2) The esters of the fatty acids in ethereal or benzene solution undergo a so-called acyloin condensation under the influence of sodium, yielding hydroxy-aldehydes containing the group ·CH(OH)·CO· united to two identical alkyl groups (C. 1906, II. 1113 : *cf.* Benzoin condensation of aromatic aldehydes, Vol. II). The reaction-mechanism of the acyloin condensation is discussed in Ann. **434,** 265.

$$2R{\cdot}COOEt + 4Na \longrightarrow 2NaOEt + R{\cdot}C(ONa) : C(ONa){\cdot}R \longrightarrow R{\cdot}CH(OH){\cdot}CO{\cdot}R$$

(3) The esters of the olefine glycols produced by the action of sodium on acid chlorides (see p. 365) yield acyloins on hydrolysis.

$$4R{\cdot}COCl + 4Na \longrightarrow 4NaCl + R{\cdot}C(O{\cdot}COR) : C(O{\cdot}COR){\cdot}R \longrightarrow R{\cdot}CH(OH){\cdot}CO{\cdot}R$$

(4) The organomagnesium compounds produced by the action of magnesium alkyl halides on aldehyde or ketone cyanohydrins yield secondary and tertiary ketone alcohols on decomposition with water or dilute acids (Compt. rend. **152,** 1100, 1256) :

$$R{\cdot}CH(OH){\cdot}CN \xrightarrow{MgR'Br} R{\cdot}CH(OMgBr){\cdot}CR' : NMgBr \longrightarrow R{\cdot}CH(OH){\cdot}CO{\cdot}R'.$$

(5) Tertiary keto alcohols are obtained by the action of magnesium alkyl halides on the monophenylhydrazones of α-diketones, followed by hydrolysis of the product (Ber. **44,** 403).

Acetylmethylcarbinol, *dimethylketol, acetoin, butan-β-ol-γ-one,* $CH_3CH(OH)COCH_3$, b.p. 148°, is produced in small quantities from acetic ester in ethereal or benzene solution by means of sodium. Also, from methyl chloroethyl ketone, $CH_3COCHClCH_3$; from βγ-butylene glycol (p. 363) by the action of the *Sorbose bacterium* or *Mycoderma aceti* ; and from various carbohydrates by the *Bacillus tartricus* (C. 1901, I. 878 : 1905, II. 117 : 1906, II. 1113). It is prepared from diacetyl (p. 402) by reduction with zinc and sulphuric acid (Ber. **40,** 4338). It polymerizes spontaneously to a *dimeric form,* $(C_4H_8O_2)_2$, m.p. 95° (Ber. **40,** 4336 : **63,** 416).

Acetylethylcarbinol, *pentan-γ-ol-β-one,* $Me{\cdot}CO{\cdot}CH(OH){\cdot}Et$, b.p. 77°/35 mm., is obtained from pentane-βγ-dione (Ber. **23,** 2425).

Propionylmethylcarbinol, *pentan-β-ol-γ-one,* $Et{\cdot}CO{\cdot}CH(OH){\cdot}Me$, b.p. 63°/20 mm., is obtained according to method 4.

Acetyldimethylcarbinol, *trimethylketol, β-methylbutan-β-ol-γ-one,* $Me{\cdot}CO{\cdot}C(OH)Me_2$, b.p. 142°, is obtained by method 5.

According to the above methods, 2 and 3, the following compounds can also be prepared : **Propionoin,** $C_2H_5COCH(OH)C_2H_5$, b.p. 73°/20 mm. **Butyroin,** b.p. 85°/10 mm. iso**Butyroin,** b.p. 83°/26 mm. **Valeroin,** b.p. 156°/12 mm. **Pivaloin,** $(CH_3)_3CCO{\cdot}CH(OH)C(CH_3)_3$, m.p. 81°, b.p. 80°/10 mm. **Capronoin,** b.p. 131°/8 mm. These keto-alcohols are reduced by sodium and alcohol partially to the glycols and partially to secondary alcohols. Heated with finely divided copper they yield α-diketones ; concentrated potassium hydroxide solution with atmospheric oxygen converts them partially to tertiary alcohol acids (comp. the *Benzilic acid transformation,* Vol. II) (C. 1906, II. 1114 : Ber. **31,** 1217).

β- or 1 : 3-*Ketols*

β-Acetoethyl Alcohol, *Butan-α-ol-γ-one,* $CH_3{\cdot}CO{\cdot}CH_2CH_2OH$, b.p. 110°/30 mm., is obtained by condensation of acetone with formaldehyde under the action of mild alkalis (D.R.P. 223207 : C. 1910, II. 347). On keeping, it polymerizes.

When the aldol condensation (p. 390) is carried out with aldehyde or chloral and acetone, methyl ethyl ketone and methyl *iso*propyl ketone by means of potassium cyanide, the following compounds result (Ber. **25,** 3165 : C. 1897, I. 1018 : 1905, II. 752) : *Hydracetylacetone,* δ-hydroxy-β-ketopentane, $CH_3CH(OH){\cdot}CH_2{\cdot}COCH_3$, b.p. 176°. *Chloralacetone,* $CCl_3CH(OH)CH_2COCH_3$, m.p. 75°.

γ-Methylpentan-β-ol-δ-one, $CH_3CH(OH)CH(CH_3)COCH_3$, b.p. 187°. *γγ-Dimethylpentan-β-ol-δ-one*, $CH_3CH(OH)C(CH_3)_2COCH_3$, b.p. 80°/10 mm., gives on oxidation *meso*-dimethylacetylacetone (p. 403).

Diacetone alcohol, $(CH_3)_2C(OH)CH_2COCH_3$, b.p. 164°, is obtained from diacetonamine (p. 274) and nitrous acid; also when two molecules of acetone are condensed by concentrated sodium hydroxide solution (Z. physik. Chem. **33**, 129) or calcium hydroxide (J.A.C.S. **31**, 722: D.R.P. 229678: C. 1911, I. 275), or by treating mesityl oxide with cold 1% hydrochloric acid (Meerwein). When heated with alkali or treated with fairly concentrated acid it is hydrolysed into two molecules of acetone.

Mesityl oxide sesquimercaptol, $(CH_3)_2C(SC_2H_5)CH_2\cdot C(SC_2H_5)_2CH_3$, can be looked on as being a derivative of diacetone alcohol. It is prepared from mesityl oxide, mercaptan, and HCl, and is an oil. Oxidation changes it into the *trisulphone*, $(CH_3)_2C(SO_2C_2H_5)\cdot CH_2\cdot C(SO_2C_2H_5)_2CH_3$, m.p. 100° (Ber. **34**, 1398). A series of further derivatives of diacetone alcohol, such as diacetone hydroxylamine, β-nitroso- and β-nitro-*iso*propyl acetone have been dealt with (p. 275) in connection with mesityl oxide.

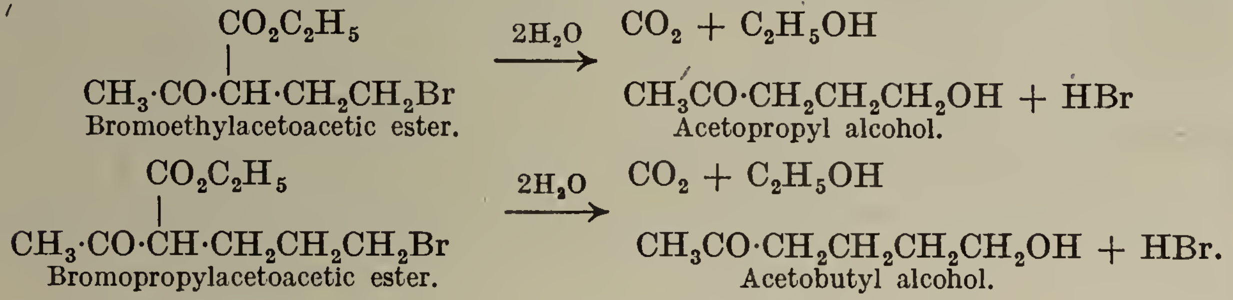
The 1:3-ketoalcohols pass into unsaturated ketones when dehydrated. Thus, diacetone alcohol yields mesityl oxide (p. 273). In the case of *gem*-dialkyl compounds, this reaction is sometimes accompanied by migration of an alkyl group (C. 1908, II. 395):

$$CH_2OH\cdot CMe_2\cdot CO\cdot Et \longrightarrow Me\cdot CH : CMe\cdot CO\cdot Et + H_2O.$$

β-Acyloxyketones are obtained synthetically by treatment of β-acyloxyacid chlorides with zinc alkyls (C. 1908, I. 1530: 1909, I. 638).

γ- or 1:4-Ketols and δ- or 1:5-Ketols

Representatives of these are obtained from the products of reaction of ethylene bromide and trimethylene bromide on sodium acetoacetic ester, by boiling with hydrochloric acid (Ber. **19**, 2844: **21**, 2647: **22**, 1196, R. 572):



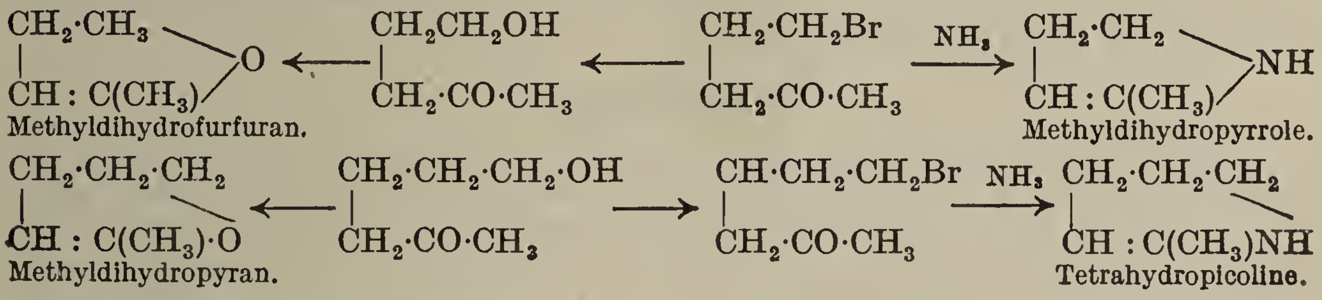
$$\underset{\text{Bromoethylacetoacetic ester.}}{CH_3\cdot CO\cdot \overset{\overset{\displaystyle CO_2C_2H_5}{|}}{C}H\cdot CH_2CH_2Br} \xrightarrow{2H_2O} \underset{\text{Acetopropyl alcohol.}}{\overset{\displaystyle CO_2 + C_2H_5OH}{CH_3CO\cdot CH_2CH_2CH_2OH + HBr}}$$

$$\underset{\text{Bromopropylacetoacetic ester.}}{CH_3\cdot CO\cdot \overset{\overset{\displaystyle CO_2C_2H_5}{|}}{C}H\cdot CH_2CH_2CH_2Br} \xrightarrow{2H_2O} \underset{\text{Acetobutyl alcohol.}}{\overset{\displaystyle CO_2 + C_2H_5OH}{CH_3CO\cdot CH_2CH_2CH_2CH_2OH + HBr.}}$$

γ-Acetopropyl alcohol, $CH_3\cdot CO\cdot CH_2CH_2CH_2OH$, b.p. 208°, with decomposition (C. 1903, II. 551).

δ-Acetobutyl alcohol, $CH_3\cdot CO(CH_2)_3CH_2OH$, or $\underbrace{CH_3\cdot C(OH)\cdot[CH_2]_3\cdot CH_2}_{O}$, dec. about 155°. *Methyl semiacetal*, b.p. 76°/99 mm. (Ber. **55**, 1390).

Both these compounds lose water when heated and form oxides of olefine glycols (see below). They do not reduce an ammoniacal copper solution, but yield the corresponding ketonic acids, lævulinic and γ-acetobutyric, when oxidized with chromic acid. On reduction they yield the corresponding glycols. Hydrobromic acid converts them into *methyl bromopropyl ketone*, $CH_3\cdot CO\cdot CH_2CH_2CH_2Br$, and *methyl bromobutyl ketone*, $CH_3\cdot CO\cdot CH_2CH_2CH_2CH_2Br$, b.p. 216°. These bromides are converted by ammonia into cyclic imides (Ber. **25**, 2190), similarly to the γ-diketones (p. 404). This reaction links the open, aliphatic compounds with the pyrrole and pyridine derivatives:



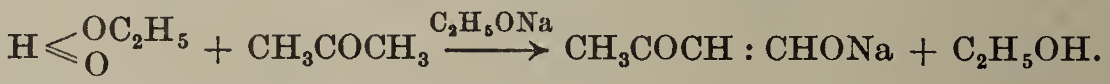
γ-Methyl-γ-acetobutyl alcohol, see Ber. **32**, 61.

Hexan-β-ol-ε-one, $Me\cdot CO\cdot[CH_2]_2CH(OH)Me$, see Ber. **42**, 1960.

B. OLEFINE KETOLS

Methoxymesityl oxide, $(CH_3)_2C : C(OCH_3)COCH_3$, b.p. 168°, and *acetoxymesityl oxide*, $(CH_3)_2C : C(OCOCH_3){\cdot}COCH_3$, b.p. 74°/12 mm., are derived from an olefine α-ketol, and are prepared from bromomesityl oxide. Hydrolysis produces acetoxymesityl oxide and acetyl*iso*butyryl respectively (p. 402) (Ber. **33**, 500).

Hydroxymethylene Ketones.—Compounds of this class are obtained from the ketones $R{\cdot}CO{\cdot}CH_3$ and $R{\cdot}CO{\cdot}CH_2R'$ and formic ester in the presence of sodium ethoxide, accompanied by the loss of alcohol:



$$H{<}^{OC_2H_5}_{O} + CH_3COCH_3 \xrightarrow{C_2H_5ONa} CH_3COCH : CHONa + C_2H_5OH.$$

These substances were at first thought to be β-keto-aldehydes. However, their pronounced acid character has shown that they should be regarded as the tautomeric hydroxymethylene ketones (*Claisen*, Ber. **20**, 2191 : **21**, R. 915 : **22**, 533, 3273 : **25**, 178). These compounds can be described as *aci*-aldehyde ketones or *aci*-formyl ketones (comp. p. 50). They dissolve in alkali carbonate solutions forming stable salts, and give green-coloured precipitates with copper acetate (Ber. **22**, 1018). Acetic anhydride and benzoyl chloride convert them readily into neutral acetates and benzoates, insoluble in alkalis. Their alkali derivatives and ethyl iodide yield *ethoxymethylene ketones*, which are saponified by alcoholic alkalis, like the ethers of organic carboxylic acids. These compounds, $—CO{\cdot}CH{=}CH{\cdot}OH$, are exceptions to the rule of Erlenmeyer (p. 46), according to which the complex $>C{=}CHOH$ present in open chains becomes rearranged into the aldehyde form $>CH{\cdot}CHO$.

The alkoxymethylene group—*e.g.* $C_2H_5O{\cdot}CH$:—may be introduced by means of orthoformic ester and acetic anhydride into compounds which contain the grouping, $—CO{\cdot}CH_2{\cdot}CO—$ (Ber. **26**, 2729), *e.g.* into acetylacetone, acetoacetic ester and malonic ester. The compounds which result will be described subsequently in their proper places.

Hydroxymethyleneacetone, aci-*formyl acetone*, aci-*acetoacetic aldehyde*, $CH_3CO{\cdot}CH{=}CHOH$, b.p. about 100°, readily condenses in solution to 1 : 3 : 5-triacetylbenzene, $C_6H_3(CO{\cdot}CH_3)_3$ (*q.v.*). Hydrazine converts it into 3-methylpyrazole, and phenylhydrazine into 1-phenyl-3-methylpyrazole (*q.v.*). **Hydroxymethylenediethyl ketone**, $C_2H_5CO{\cdot}C(CH_3){=}CHOH$, m.p. 40°, b.p. 164–166°. *aci*-**Diethylacetylacetaldehyde**, $(C_2H_5)_2CHCOCH : CHOH$, b.p. 174°. *aci*-**Trimethylacetylacetaldehyde**, $(CH_3)_3CCOCH : CHOH$, b.p. 148°. *aci*-*iso*-**Valerylacetaldehyde**, $(CH_3)_2CH{\cdot}CH_2COCH : CHOH$, b.p. 52°/10 mm. *aci*-*iso*-**Caproylacetaldehyde**, $C_5H_{11}COCH : CHOH$, cannot be distilled without decomposition even *in vacuo* (C. 1905, II. 393).

Diolefine ketols, such as $CMe_2 : CH{\cdot}CO{\cdot}CH : CHOH$, are obtained by condensing unsaturated ketones with formic esters (Compt. rend. **150**, 705).

NITROGEN-CONTAINING DERIVATIVES OF THE KETONE-ALCOHOLS

As in the case of the simple ketones, the ketone-alcohols can frequently be characterized through their semicarbazones, oximes, and phenylhydrazones (comp. pp. 268, 269). It has, however, already been pointed out that the α-ketols, combining with phenylhydrazine, easily yield the osazones of the α-diketones. The β-hydroxymethylene ketones react with hydroxylamine and hydrazine, as do the β-diketones (p. 407) forming the cyclic compounds isoxazoles and pyrazoles.

Those derivatives of the ketone-alcohols, in which the hydroxyl group has been replaced by a nitrogen group, have been most conveniently collected into the following series of compounds.

Nitroketones

Nitroacetone, $CH_3COCH_2{\cdot}NO_2$, b.p. 152°, is prepared by oxidation of nitro*iso*propyl alcohol (Ber. **32**, 865). An apparently isomeric *nitroacetone*, m.p. 49°, is obtained from iodo-acetone and silver nitrite (Ber. **32**, 3179); both substances are acid in character. Aniline reacts with nitroacetone (m.p. 49°) forming the *anil*, $CH_3C(:NC_6H_5)CH_2NO_2$, m.p. 87°, which can also be obtained from nitritomesityl dioxime peroxide (p. 275) and aniline acetate (Ann. **319**, 230). On nitro*iso*propylacetone, see p. 275.

ββ-Chloronitropropanol, $CH_3{\cdot}CCl(NO_2){\cdot}CH_2OH$, m.p. 13°, b.p. 115°/44 mm., is obtained from αα-chloronitroethane and formaldehyde. *ββ-Bromonitropropanol*, m.p. 42°.

ββ-Chloronitro-α-butanol, $C_2H_5{\cdot}CCl(NO_2){\cdot}CH_2OH$, b.p. 145–150° (C. 1897, II. 338 : 1898, I. 194).

ββγ-Trinitro-β-methylbutane, $Me_2C(NO_2){\cdot}C(NO_2)_2Et$, m.p. 95°, is obtained from *iso*pentane and nitric acid (Ber. **32**, 1443).

Aminoketones

Saturated aminoketones are obtained by the action of ammonia or amines on the halogen ketones. Aminoketones (chiefly the β-derivatives) are also obtained by the addition of ammonia to αβ-olefine ketones and α-aminoketones are obtained by the reduction of *iso*nitrosoketones with stannous chloride (Ber. **30**, 1515 : **32**, 1095).

Aminoacetone, $CH_4{\cdot}CO{\cdot}CH_2NH_2$, is formed by the reduction of *iso*nitrosoacetone or of nitroacetone (m.p. 49°). Its hydrochloride is obtained by heating with hydrochloric acid the compound $C_6H_{10}N_2$ which is obtained by the hydrolysis of phthalimidoacetone (Ber. **38**, 752).

Dimethylaminoacetone, $CH_3{\cdot}CO{\cdot}CH_2NMe_2$, b.p. 123°. *Diethylaminoacetone*, b.p. 153° (Ber. **29**, 866). *Acetonyltrimethylammonium chloride*, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}NMe_3Cl$, *coprin*, is formed from chloroacetone and trimethylamine. It has a physiological action similar to that of curare (C. 1898, II. 631).

Aminosulphonal, *aminoacetonediethyl sulphone*, $NH_2{\cdot}CH_2{\cdot}C(SO_2Et)_2{\cdot}CH$, m.p. 94°, is obtained by the hydrolysis of phthalimidosulphonal. The latter is obtained by the oxidation of the ethylmercaptole formed from phthalimidoacetone, ethyl mercaptan and hydrochloric acid (Ber. **32**, 2749).

By the action of mercuric chloride the α-aminoketones are oxidized to pyrazine derivatives, *e.g.* aminiacetone yields dimethylpyrazine (Ber. **27**, R. 928). The aminoketone hydrochlorides react with potassium cyanate to form iminazolones, while potassium thiocyanate yields thioliminazoles. These heterocyclic compounds are described in Vol. III (*cf.* Ber. **27**, 1942, 2036).

Unsaturated β-aminoketones are obtained by the action of ammonia or amines on acetylacetone (p. 403) (Ber. **26**, R. 290). *Acetylacetoneamine*, $CH_3{\cdot}CO{\cdot}CH : C(NH_2){\cdot}CH_3$, m.p. 43°, b.p. 209°. *Acetylacetoneethyl-* and *-diethylamines*, $CH_3{\cdot}CO{\cdot}CH : C(NHEt \text{ or } NEt_2){\cdot}CH_3$, b.p. 210–215° and 155°/24 mm.

Triacetonyltriaminetrioxime, $N(CH_2{\cdot}C(: NOH){\cdot}CH_3)_3$, m.p. 184°, is obtained from chloroacetone oxime and ammonia (Ber. **31**, 2396).

DIALDEHYDES, KETOALDEHYDES AND DIKETONES

The dialdehydes, ketone aldehydes, and diketones constitute a closely united series of compounds, connected together by many characteristics. They are subdivided according to the position of the two CO groups relatively to each other : α- or 1 : 2-, β- or 1 : 3-, γ- or 1 : 4-, δ- or 1 : 5-, diketo-compounds, of which the characteristic reactions will be described amongst the diketones (pp. 401 *et seqq.*).

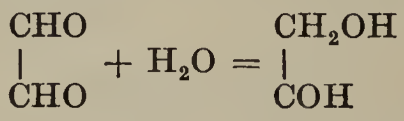
4. DIALDEHYDES

Glyoxal, *oxaldehyde, diformyl* [ethane-dial], $CHO{\cdot}CHO$, m.p. about 15°, b.p. 51°, $D_{20} = 1{\cdot}14$, was discovered by *Debus* in 1856. It is the dialdehyde of ethylene glycol and of oxalic acid.

Glyoxal, glycollic acid and glyoxylic acid are formed by the careful oxidation of ethylene glycol, ethyl alcohol (Ber. **14**, 2685 : **17**, R. 168), or acetaldehyde with nitric acid. It can also be formed from dihydroxytartaric acid by the interaction of its sodium salt and sodium bisulphite (Ber. **24**, 3235). It is best obtained from " glyoxal sulphate " (*q.v.*), which is obtained technically by the action of fuming sulphuric acid on tetrahalogenethanes, by heating with water (D.R.P. 362743 : C. 1923, II. 743). Acetylene is converted by very dilute ozone into glyoxal (Chem. Ztg. **44**, 157). Glyoxal is also obtained by the breakdown of $\alpha\beta$-unsaturated aldehydes by ozone, and can thus be prepared by warming cinnamaldehyde ozonide (see Vol. II) with water.

By this means a *trimeric* glyoxal $(CHO{\cdot}CHO)_3$ is obtained, whilst the other methods result in the production of a polymeric *paraglyoxal*, $(CHO{\cdot}CHO)_n$, when the aqueous solution of glyoxal is evaporated. This amorphous powder melts with difficulty. When heated with P_2O_5 it is converted into the *monomolecular* glyoxal, in the form of golden yellow crystals and a yellow-green vapour, with the pungent odour of formaldehyde. It dissolves in non-aqueous solvents to a yellow solution. The colours are characteristic, since *all bodies which contain the α-diketo-group* —CO·CO— *possess a more or less strongly developed colour*, usually yellow to orange. In a small quantity of water glyoxal polymerizes to paraglyoxal ; in more water, it dissolves with a generation of heat to the monomolecular colourless hydrate, $HCO{\cdot}CH(OH)_2$ or $(HO)_2CH{\cdot}CH(OH)_2$. The aqueous solutions of the various modifications all give the same reactions, except with Fehling's solution, which is reduced only by the trimeric glyoxal (Harries, Ber. **40**, 165).

Reactions.—The alkalis convert it, even in the cold, into glycollic acid. In this change the one CHO group is reduced, whilst the other is oxidized (comp. Benzil and Benzilic acid, Vol. II) :

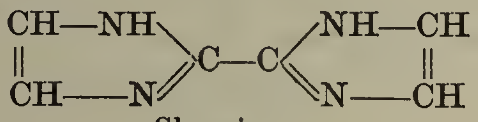


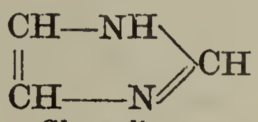
$$\begin{array}{c} CHO \\ | \\ CHO \end{array} + H_2O = \begin{array}{c} CH_2OH \\ | \\ COH \end{array}$$

It reduces ammoniacal silver solution with the formation of a mirror, and unites with two molecules of sodium hydrogen sulphite to form a crystalline *glyoxal sodium sulphite,* $C_2H_2O_2(SO_3HNa)_2 + H_2O$. Ethyl alcohol and a little HCl give rise to *glyoxal tetraethyl acetal,* $(C_2H_5O)_2CH{\cdot}CH(OC_2H_5)_2$, b.p. 89°/14 mm. (Ber. **40**, 171). Similarly, glyoxal and glycol form *glyoxal diethylene acetal,* $C_2H_4 : O_2CH{\cdot}CHO_2 : C_2H_4$, m.p. 134° (Ber. **28**, R. 321).

Glyoxal bisulphite reacts smoothly with primary and secondary amines to form glycine derivatives or indolesulphonic acids (Vol. III), according to the nature of the reacting base (Ber. **27**, 3258).

Glyoxal reacts with concentrated ammonia with the formation of the two heterocyclic bases glycosine (Ann. **456**, 253) and glyoxaline (Ann. **277**, 336). Glyoxaline is formed more easily from glyoxal, two mols. of ammonia and formaldehyde (see Vol. III).


Glycosine.


Glyoxaline.

Glyoxal reacts with *o*-phenylenediamine like the α-diketones (p. 401) with formation of quinoxaline.

Glyoxal combines with two molecules of hydrocyanic acid to yield the dinitrile of racemic acid.

On the condensation of glyoxal with malonic ester and acetoacetic ester, see Ber. **21**, R. 636.

Glyoxime (see p. 407), *glyoxal osazone* (see p. 409). Urea combines with glyoxal to form glycoluril (*q.v.*), a diureide.

Acetaldehydedisulphonic acid, $CHO\cdot CH(SO_3H)_2$, can be considered as being a derivative of glyoxal. It is prepared (1) in the form of its bisulphite compound, when chloral is warmed with potassium sulphite ; (2) by the saturation of fuming sulphuric acid with acetylene (comp. pp. 110, 247); (3) by the action of fuming sulphuric acid on acetaldehyde (C. 1902, I. 405). By warming with alkalis it passes smoothly into the salts of formic and methionic acids (Ann. **303**, **114**). The dialkylamides of acetaldehydedisulphonic acid are obtained from sodium methionic dialkylamides and formic ester :

$$HCOOCH_2 + NaCH(SO_2NR_2)_2 \longrightarrow HCO\cdot CH(SO_2NR_2)_2 \text{ or } HOCH : C(SO_2NR_2)_2.$$

Further derivatives of glyoxal are those which result from the action of 2HClO, 2HBrO, and $2Br_2$ on acetylene—*dichloroacetaldehyde*, $CHCl_2CHO$, *dibromoacetaldehyde*, $CHBr_2CHO$ (comp. p. 240).

Malondialdehyde, $CH_2(CHO)_2$, has not yet been isolated. A derivative of its tautomeric hydroxymethylene form, CHOH : CH·CHO, is *ethoxyacrolein acetal*, $EtO\cdot CH : CH\cdot CH(OEt)_2$, which is obtained by heating propargyl acetal with alcoholic sodium ethoxide. Similarly, the derivative *β-anilinoacrolein anil*, $C_5H_5NHCH : CH\cdot CH : NC_6H_5$, is obtained from propiolaldehyde and aniline hydrochloride (Ber. **36**, 3668).

Propane tetraethyl sulphone, $CH_2[CH(SO_2C_2H_5)_2]_2$, m.p. 154°, is derivable from malonic dialdehyde, and is synthetically prepared by the condensation of formaldehyde with two molecules of methylene diethyl sulphone (p. 247) (Ber. **33**, 1123).

Succindialdehyde [butanedial], $CHO\cdot CH_2\cdot CH_2\cdot CHO$, b.p. 67°/10 mm., can be obtained from diallyl (p. 117) by means of ozone ; but is most conveniently prepared by the action of N_2O_3 on its dioxime (p. 408), which is obtained from pyrrole. It is isomeric with butyrolactone (p. 427), and can be looked on as being a hydrate of furfuran, from which it can be obtained by the action of HCl in methyl alcohol, in the form of its *tetramethyl acetal*, $CH(OCH_3)_2CH_2CH(OCH_3)_2$, b.p. 202°. The *tetraethyl acetal*, b.p. 116°/20 mm., results from the electrolysis of the sodium salt of β-diethoxypropionic acid $(C_2H_5O)_2CHCH_2COOK$ (Ber. **39**, 891). Succindialdehyde polymerizes readily to a glassy substance from which it is regenerated on distillation (Harries, Ber. **35**, 1183 : **39**, 3670). When heated with water it forms furfuran, with ammonia pyrrole, and with P_2S_3 thiophene (comp. 1 : 4-Diketones, p. 404).

Dibromosuccinaldehyde, HCO·CHBr·CHBr·CHO, m.p. 73°, is prepared from the aldehyde and bromine. *Bromofumaraldehyde*, HCO·CH : CBrCHO, b.p. 130°/15 mm., is obtained by distillation of the previous compound.

On the breaking down of furfuran into *nitrosuccinaldehyde*, and the conversion of the latter, by boiling with water, into *fumaric dialdehyde*, CHO·CH : CH·CHO, see C. 1902, I. 1272.

Maleinaldehyde tetraethylacetal is more readily accessible by reduction of the easily available acetylenedialdehyde diacetal (Ber. **45**, **340**).

Dibromomaleinaldehyde, $\mathrm{CHO{\cdot}CBr : CBr{\cdot}CHO}$, m.p. 69°, is obtained from $\beta\gamma$-dibromopyrotartaric acid and bromine water (Ann. **232**, 89).

Glutaric aldehyde, $\mathrm{CHO{\cdot}[CH_2]_3{\cdot}CHO}$, b.p. 188°/760 mm., is obtained by decomposition of *cyclo*pentanone ozonide. It forms a glassy polymer under the action of traces of water, and is volatile in steam (Ber. **41**, 1705).

Homologues of glutaric aldehyde are obtained by condensing aliphatic aldehydes with unsaturated aldehydes of the acrolein type by sodium ethoxide in alcoholic solution (*Meerwein*, Ber. **53**, 1829). By prolonged action of the sodium ethoxide, the dialdehydes undergo isomerization into δ-lactones, *e.g* :

$$\begin{array}{c}\mathrm{Et{\cdot}CH : CMe{\cdot}CHO}\\ + \\ \mathrm{CHMe_2{\cdot}CHO}\end{array} \longrightarrow \begin{array}{l}\mathrm{Et{\cdot}CH{\cdot}CHMe{\cdot}CHO}\\ | \\ \mathrm{CMe_2{\cdot}CHO}\end{array}$$

(see p. 428).

The higher dialdehydes, from adipic aldehyde upwards, can be synthesized from the polymethylene diiodides, by converting them into the dinitro compounds with silver nitrite, reducing these to the dioximes and hydrolysing the latter (*v. Braun*, Ber. **44**, 2526 : **46**, 103).

Adipic dialdehyde [*hexanedial*], $\mathrm{CHO{\cdot}[CH_2]_4CHO}$, b.p. 93°/9 mm., is obtained from α, α_1-dihydroxysuberic acid by oxidation with $\mathrm{PbO_2}$. Its *tetraethylacetal*, $\mathrm{(EtO)_2CH{\cdot}[CH_2]_4{\cdot}CH(OEt)_2}$, b.p. 148°/10 mm., results from the electrolysis of the potassium salt of γ-diethoxybutyric acid. The aldehyde polymerizes more slowly than the higher and lower homologues, although heating with water condenses it rapidly to *cyclo*pentenaldehyde (Vol. II) (Ber. **39**, 891).

Pimelic aldehyde (*heptanedial*), $\mathrm{CHO{\cdot}[CH_2]_5{\cdot}CHO}$, b.p. 110–112°/33 mm. (Ber. **46**, 108) ; *Disemicarbazone*, m.p. 183°.

Suberic dialdehyde, *octanedial*, $\mathrm{CHO[CH_2]_6CHO}$, b.p. 142°/30 mm., is prepared from dihydroxyadipic acid and $\mathrm{PbO_2}$. It polymerizes very easily (Ber. **31**, 2106).

The oximes, hydrazones and osazones of the dialdehydes are described together with the corresponding compounds of the aldehyde-ketones and diketones (p. 406).

Acetylenedialdehyde diacetal, $\mathrm{(EtO)_2CH{\cdot}C : C{\cdot}CH(OEt)_2}$, b.p. 125–128°/11 mm., is obtained by the action of orthoformic ester on acetylene dimagnesium bromide (Ber. **45**, 339).

5. KETOALDEHYDES

α-Ketoaldehydes.—Pyruvic aldehyde, *methylglyoxal* [propanalone], $\mathrm{CH_3{\cdot}CO{\cdot}CHO}$, is a yellow volatile oil which is liberated from its monoxime, *iso*nitrosoacetone by dilute acids. It is also obtained by ozonolysis of mesityl oxide, and by the action of alkalis on glucose (J. Biol. Chem. **15**, 127). It is probably an intermediate product in the alcoholic fermentation of hexoses (p. 140). It is most readily prepared by heating dihydroxyacetone with three times its weight of phosphorus pentoxide (Ber. **57**, 1502). It polymerizes very easily.

Methylglyoxal acetal, $\mathrm{Me{\cdot}CO{\cdot}CH(OEt)_2}$, b.p. 30°/10 mm. (Ber. **38**, 1630).

Derivatives include *dichloroacetone*, $\mathrm{CH_3COCHCl_2}$, b.p. 120° (comp. p. 265), produced from allylene and 2HClO. *Dibromoacetone*, $\mathrm{CH_3COCHBr_2}$, b.p. 142°, results from allylene and 2HBrO. Similarly, *dichloropinacolin*, $\mathrm{(CH_3)_3C{\cdot}CO{\cdot}CHCl_2}$, m.p. 51°, and *dibromopinacolin*, $\mathrm{(CH_3)_3C{\cdot}COCHBr_2}$, m.p. 75°, are obtained from *tert.*-butyl acetylene. These are derivatives of tert.*-butylglyoxal* (C. 1900, II. 29).

Propanal disulphonic acid, $\mathrm{CH_3C(SO_3H)_2CHO}$, is prepared from propionic aldehyde and fuming sulphuric acid (C. 1902, I. 405).

*iso***Propylglyoxal** [γ-methyl-butanal-β-one], $\mathrm{(CH_3)_2CH{\cdot}COCHO}$, m.p. 95°, is produced from the acid $\mathrm{CHO{\cdot}CO{\cdot}C(CH_3)_2{\cdot}COOH}$ by fusion or by boiling with water (Ber. **30**, 861).

β-Ketoaldehydes, such as formyl acetone, $\mathrm{CH_3{\cdot}COCH_2CHO}$, have already been described (p. 396), since in the free state they assume the *aci-* configuration, which leads to their inclusion with the β-hydroxymethylene ketones.

γ-Ketoaldehydes.—Lævulinic aldehyde [pentanal-4-one], $\mathrm{CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2CHO}$, b.p. 187°/760 mm., b.p. 70°/12 mm., is obtained from its *methylal*, b.p. 86°/13 mm., the reaction product of a boiling solution of hydrochloric acid in methyl alcohol on α-methyl furfural or sylvan (Ber. **31**, 37).

δ-Ketoaldehydes are obtained by condensation of aldehydes with αβ-unsaturated ketones under the action of sodium ethylate, and readily isomerize to δ-lactones (see Glutaric aldehyde and p. 428).

6. DIKETONES

The relative position of the CO-groups determines them to be either α- or 1 : 2-diketones, β- or 1 : 3-diketones, γ- or 1 : 4-diketones, etc.

The α-diketones are most generally designated as compounds of two acid radicals, *e.g.* diacetyl for $CH_3CO\cdot COCH_3$; the β-diketones as acyl ketones, *e.g.* acetyl acetone, $CH_3CO\cdot CH_2\cdot CO\cdot CH_2$.

The diketones react like the monoketones with hydroxylamine and phenylhydrazine. Their oximes, prepared in another manner, constitute the chief raw material from which to prepare the α-diketones. The nitrogen-containing derivatives of the diketones, the aldehyde ketones and dialdehydes will be discussed after the diketones, because of their greater convenience in this position.

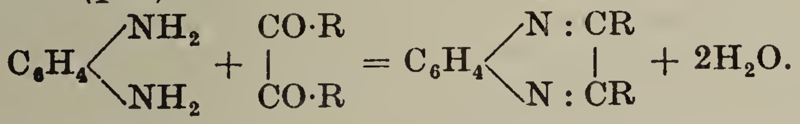
For the mercaptole and sulphone formation of the diketones, see Ber. **35**, 493.

(1) α- or 1 : 2-Diketones

These are obtained (1) from their monoximes, the *iso*nitrosoketones, by boiling the latter with dilute sulphuric acid (v. Pechmann) (Ber. **20**, 3213 : **21**, 1411 : **22**, 527, 532 : **24**, 3954 : C. 1904, II. 1701); (see pyroracemic aldehyde). They are also formed (2) by the oxidation of the α-ketols, *e.g.* the synthetic acyloins by atmospheric oxygen; and (3) accompanied by dinitroparaffins (p. 185), when monoketones or the corresponding secondary alcohols are oxidized by nitric acid (Ber. **28**, 555 : C. 1900, II. 624 : 1901, II. 334); (4) from α-bromoolefine ketones containing the group —C : CBr·CO—, instead of the expected α-olefine ketone-alcohols (p. 396) (Ber. **34**, 2092).

The α-diketones, in contradistinction to the colourless aliphatic monoketones, are yellow, volatile liquids with a penetrating quinone-like odour; comp. glyoxal (p. 398). On the absorption spectra of α-diketones, see C. 1906, II. 495.

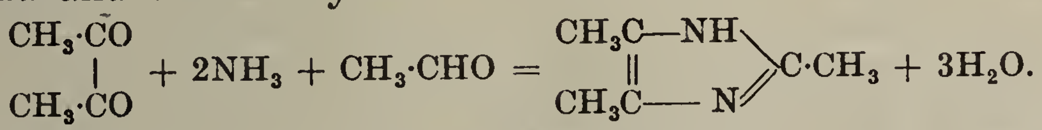
(1) The α-diketones are characterized and distinguished from the β- and γ- diketones by their ability to unite with the *ortho*phenylenediamines (similarly to glyoxal). In this way they are condensed to the quinoxalines (*q.v.*):



$$C_6H_4\left\langle\begin{array}{l}NH_2\\ \\ NH_2\end{array}\right. + \begin{array}{l}CO\cdot R\\ |\\ CO\cdot R\end{array} = C_6H_4\left\langle\begin{array}{l}N:CR\\ \quad\ |\\ N:CR\end{array}\right. + 2H_2O.$$

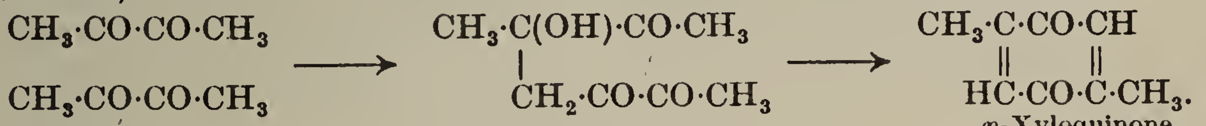
All compounds containing the group —CO·CO—, *e.g.* glyoxal, pyroracemic acid, glyoxylic acid, alloxan, dihydroxytartaric acid, etc., react similarly with the *o*-phenylenediamines.

(2) Glyoxalines are formed by the interaction of α-diketones with ammonia and the aldehydes:



$$\begin{array}{l}CH_3\cdot CO\\ \quad |\\ CH_3\cdot CO\end{array} + 2NH_3 + CH_3\cdot CHO = \begin{array}{l}CH_3C—NH\\ \quad \|\\ CH_3C—N\end{array}\!\!\!\!\!\!\!\!>C\cdot CH_3 + 3H_2O.$$

(3) α-Diketones, containing a CH_2-group, adjacent to the CO-group, undergo a rather remarkable condensation when acted on by the alkalis. Aldols are first produced, and later quinones (Ber. **22**, 2215 : **28**, 1845):



$$\begin{array}{l}CH_3\cdot CO\cdot CO\cdot CH_3\\ \\ CH_3\cdot CO\cdot CO\cdot CH_3\end{array} \longrightarrow \begin{array}{l}CH_3\cdot C(OH)\cdot CO\cdot CH_3\\ \qquad |\\ \qquad CH_2\cdot CO\cdot CO\cdot CH_3\end{array} \longrightarrow \begin{array}{l}CH_3\cdot C\cdot CO\cdot CH\\ \qquad \|\qquad \|\\ HC\cdot CO\cdot C\cdot CH_3.\end{array}$$

p-Xyloquinone.

(4) Diacetyl and hydrocyanic acid yield the nitrile of dimethyl racemic acid (see glyoxal) (Ber. 22, R. 137).

Diacetyl, $CH_3{\cdot}CO{\cdot}CO{\cdot}CH_3$, *diketobutane, dimethyl diketone, dimethylglyoxal* [butane-dione], is obtained (1) from *iso*nitroso-ethyl methyl ketone by the action of dilute sulphuric acid (Ber. **40**, 4337); (2) from methyl ethyl ketone or methyl ethyl carbinol by oxidation with nitric acid, accompanied by dinitro-ethane (p. 185); (3) from oxalyldiacetic or ketipic acid, $COOH{\cdot}CH_2CO{\cdot}CO{\cdot}CH_2COOH$, by elimination of $2CO_2$ by heat (Ber. **20**, 3183); (4) by oxidation of tetrinic acid (*q.v.*) by $KMnO_4$ (Ber. **26**, 2220: Ann. **288**, 27); (5) by electrolysis of pyroracemic acid, $CH_3CO{\cdot}COOH$ (Ber. **33**, 650); (6) from vinylidene oxanilide, an oxalic acid derivative, and methyl magnesium iodide (Ber. **40**, 186).

It is a yellow liquid with a quinone-like odour, b.p. 87–89°. When shaken with hydrochloric acid, diacetyl polymerizes to the trimeric $(CH_3CO{\cdot}COCH_3)_3$, m.p. 105°, b.p. 280°, which decomposes on prolonged heating (Ber. **35**, 3290: **36**, 954).

Tetrachlorodiacetyl, $CHCl_2{\cdot}CO{\cdot}CO{\cdot}CHCl_2$, m.p. 84°, results from the action of potassium chlorate on chloroanilic acid (together with tetrachloroacetone, p. 265) (Ber. **22**, R. 809: **23**, R. 20). *Tetrabromodiacetyl*, $(CHBr_2{\cdot}CO)_2$ (Ber. **23**, 35), and dibromodiacetyl, $(CH_2Br{\cdot}CO)_2$, are produced by the action of bromine on diacetyl.

Acetylpropionyl, $C_2H_5{\cdot}CO{\cdot}CO{\cdot}CH_3$, *methyl ethyl diketone* [$\beta\gamma$-pentane-dione], b.p. 108°, is obtained from *iso*nitroso-diethyl ketone; also by the hydrolysis of α-bromoethylidene acetone, $CH_3CH : CBrCOCH_3$ (Ber. **34**, 2092). It condenses to duroquinone.

Acetylbutyryl [$\beta\gamma$-hexane-dione], $C_3H_7COCOCH_3$, b.p. 128°, *acetyl*iso*butyryl*, $(CH_3)_2CHCO{\cdot}COCH_3$, b.p. 115°, results from the hydrolysis of acetoxymesityl oxide (p. 396).

Acetyl*iso*valeryl, $(CH_3)_2CHCH_2COCOCH_3$, b.p. 138°. *Acetylcaproyl*, $CH_3[CH_2]_4COCOCH_3$, b.p. 172° (C. 1898, II. 965; 1900, II. 624). *Acetyl*iso*caproyl*, $(CH_3)_2CHCH_2CH_2COCOCH_3$, b.p. 163° (Ber. **22**, 2117: **24**, 3956).

Symmetrical diketones: *Dipropionyl*, $CH_3CH_2CO{\cdot}COCH_2CH_3$. *Dibutyryl*, $CH_3CH_2CH_2CO{\cdot}COCH_2CH_2CH_3$, b.p. 168°. *Di*-iso*butyryl*, $(CH_3)_2CHCO{\cdot}COCH(CH_3)_2$, b.p. 145°. *Di*-iso*valeryl*, $(CH_3)_2CHCH_2CO{\cdot}COCH_2CH(CH_3)_2$. *Dicaproyl*, $C_5H_{11}COCOC_5H_{11}$, b.p. 110–120°/10 mm. *Dipivaloyl*, $(CH_3)_3C{\cdot}CO{\cdot}CO{\cdot}C(CH_3)_3$, b.p. 170°. All these bodies are obtained from the α-ketols (pp. 393–4), by oxidation with nitric acid or dehydration by means of finely divided copper (J. pr. Chem. [2] **62**, 364: C. 1906, II. 1115).

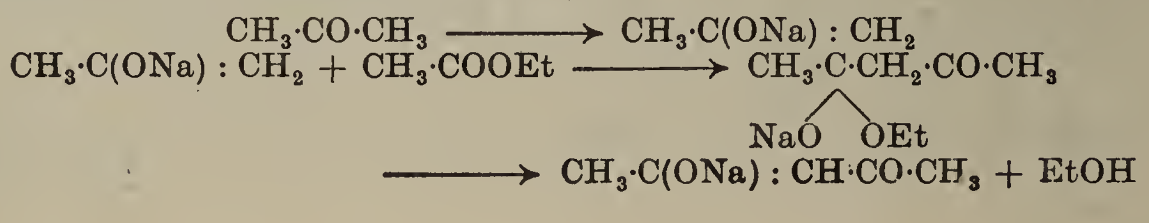
α-Diketone Dichlorides result from the action of hypochlorous acid on alkyl acetylenes (p. 112), according to the equation:

$$C_2H_5C : CCH_3 + 2HClO = C_2H_5CCl_2{\cdot}COCH_3 + H_2O.$$

Methyl α-dichloropropyl ketone, $C_2H_5{\cdot}CCl_2{\cdot}CO{\cdot}CH_3$, b.p. 138°, yields methyl *n*-propyl ketone on reduction; with potassium carbonate solution it forms duroquinone, angelic acid (p. 346), and α-ethyl acrylic acid. The two acids result from an intramolecular atomic rearrangement which recalls that of the formation of benzilic acid from benzil (p. 48).

(2) β- or 1 : 3-Diketones

These are produced according to two nucleus-synthetic reactions: (1) like the hydroxymethyleneketones, by the interaction of acetic esters and ketones in the presence of sodium ethoxide, metallic sodium or sodamide (Claisen, Ber. **22**, 1009: **23**, R. 40: **38**, 695). The condensation proceeds like the acetoacetic ester condensation (p. 467) and consists, first, of the formation of the sodium derivative of the *enolic* form of the ketone. The sodium derivative then combines with the ester, and by loss of alcohol from the resulting product, the sodium derivative of the diketone is formed.

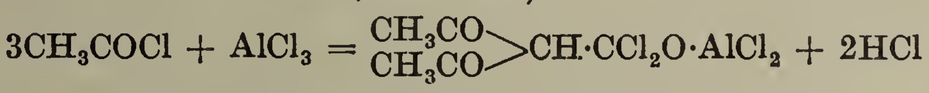


$$CH_3{\cdot}CO{\cdot}CH_3 \xrightarrow{\qquad} CH_3{\cdot}C(ONa) : CH_2$$

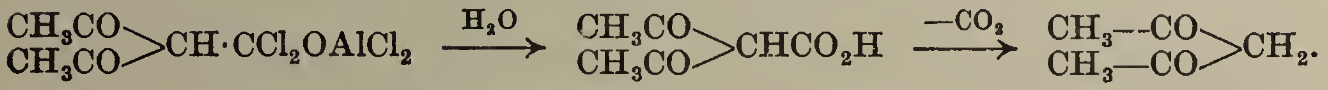
$$CH_3{\cdot}C(ONa) : CH_2 + CH_3{\cdot}COOEt \xrightarrow{\qquad} CH_3{\cdot}\underset{NaO\ \ OEt}{C}{\cdot}CH_2{\cdot}CO{\cdot}CH_3$$

$$\xrightarrow{\qquad} CH_3{\cdot}C(ONa) : CH{\cdot}CO{\cdot}CH_3 + EtOH$$

(2) By the action of $AlCl_3$ on acetyl chloride and the subsequent decomposition of the aluminium derivative. This reaction was discovered by *Combes*, but correctly interpreted by *Gustavson* (Ber. **21**, R. 252 : **22**, 1009 : C. 1901, I. 1263) :



$$3CH_3COCl + AlCl_3 = \begin{matrix} CH_3CO \\ CH_3CO \end{matrix}\!\!>CH{\cdot}CCl_2O{\cdot}AlCl_2 + 2HCl$$



$$\begin{matrix} CH_3CO \\ CH_3CO \end{matrix}\!\!>CH{\cdot}CCl_2OAlCl_2 \xrightarrow{H_2O} \begin{matrix} CH_3CO \\ CH_3CO \end{matrix}\!\!>CHCO_2H \xrightarrow{-CO_2} \begin{matrix} CH_3{-}CO \\ CH_3{-}CO \end{matrix}\!\!>CH_2.$$

(3) Acylacetoacetic esters (p. 602), when heated with water at 140–150°, decompose into CO_2, alcohol and β-diketones (C. 1903, I. 225) :

$$\begin{matrix} CH_3CH_2CH_2CO \\ CH_3CO \end{matrix}\!\!>CHCO_2C_2H_5 \xrightarrow{H_2O} \begin{matrix} CH_3CH_2CH_2CO \\ CH_3CO \end{matrix}\!\!>CH_2 + CO_2 + C_2H_5OH.$$

Constitution.—The 1 : 3 diketones resemble the hydroxymethyleneketones (p. 396) in the possession of acidic properties, but whereas the latter are usually regarded as hydroxymethylene or enolic compounds, the diketones, either free or in solution apparently exist as an equilibrium mixture of keto and enol forms, the position of equilibrium being determined by the characters of the solvent among other factors. The salts are derived from the enol form, $R{\cdot}CO{\cdot}CH : C(ONa){\cdot}R$. (*cf.* also Acetoacetic ester, p. 473, formylacetic ester, p. 456, and introduction, p. 50).

Reactions.—A very characteristic reaction is the precipitation of their alkali salts by copper acetate. Ferric chloride imparts an intense red colour to their alcoholic solution.

When the salts of β-diketones are treated with alkyl iodides, the CH_2-group becomes alkylated (comp. Acetoacetic ester) :

$$CH_3COCH_2COC_3H_7 \xrightarrow[CH_3I]{C_2H_5ONa} CH_3COCH(CH_3)COC_3H_7.$$

Hydroxylamine converts the β-diketones into isoxazoles, phenylhydrazine into pyrazoles (pp. 407, 409).

Acetylacetone, $CH_3CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3$, b.p. 137° (see above for methods of formation). Electrolysis of an alcoholic solution of sodium acetylacetone, or the action of iodine on the same body, leads to the formation of tetraacetylethane (Ber. **26**, R. 884). With S_2Cl_2 and SCl_2 it forms dithio- and monothio-acetylacetone respectively (Ber. **27**, R. 401, 789). H_2S produces a dimeric *dithioacetylacetone* $(C_5H_2S_2)_2$, m.p. 163° (C. 1901, II. 397). Cyanogen unites with acetyl acetone in presence of a little sodium ethoxide to form *cyaniminomethylacetylacetone*, $NC{\cdot}C(NH){\cdot}CH(COCH_3)_2$, m.p. 130°, and *diiminotetraacetylbutane*, $(CH_3CO)_2C(NH)C(NH)CH(COCH_3)_2$, m.p. 147° (Ber. **31**, 2938).

The *metallic salts* of acetylacetone resemble one another in their remarkable stability. Those of Be, Al, Cr, Mn, Zn, Fe, Cu, Hg, Mo, Pt″, Ce, La, Th, and others have been prepared, of which some, on account of their power of crystallization, have been employed for the determination of the valency and atomic weights of the rare elements (C. 1900, I. 588 : Ber. **34**, 2584 : Ann. **331**, 334). *Copper acetylacetone*, $Cu(C_5H_7O_2)_2$. *Beryllium acetylacetone*, $Be(C_5H_7O_2)_2$, m.p. 108°, b.p. 270°. *Aluminium acetylacetone*, $Al(C_5H_7O_2)_3$, m.p. 193°, b.p. 314°. The vapour density of these compounds reveals the divalence of Be and the trivalence of Al. *Chromium acetylacetone*, $Cr(C_5H_7O_2)_3$, b.p. 340°, is of a violet colour, and gives off a green vapour (*Coombes*, Ber. **28**, R. 10 : C. 1899, II. 525).

Octochloroacetylacetone, m.p. 53°, and *octobromoacetylacetone*, $CBr_3COCBr_2COCBr_3$, m.p. 154°, are obtained from phloroglucinol, and chlorine or bromine respectively (Vol. II) (Ber. **23**, 1717).

Alkyl acetylacetones are obtained from acetylacetone by sodium and alkyl iodides (Ber. **20**, R. 283 : **21**, R. 11).

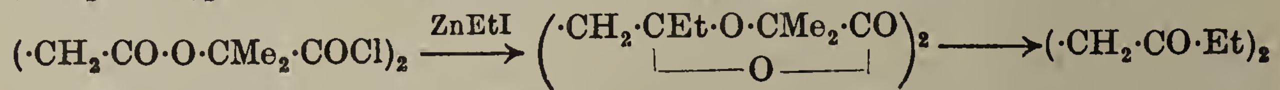
Acetylpropionylmethane, $CH_3COCH_2COC_2H_5$, b.p. 158°. *Acetylbutyrylmethane*, b.p. 175° (Ber. **22**, 1015: C. 1903, I. 225). *Acetylisobutyrylmethane*, b.p. 168° (Ber. **31**, 1342: C. 1900, II. 317). *Acetylcaproylmethane*, $CH_3[CH_2]_4COCH_2{\cdot}COCH_3$, b.p. 100°/20 mm., also results from acetylœnanthylidene (p. 276) and sulphuric acid (C. 1900, II. 1262: 1903, I. 225).

Higher β-diketones: see C. 1902, I. 568.

(3) γ- or 1 : 4-Diketones

A general method for the preparation of these ketones has been evolved, starting from succinyl chloride. The chloride of a succinoxy-fatty acid, produced from succinyl chloride and α-hydroxy*iso*butyric acid, reacts with zinc alkyls to form a dilactone, from which the desired diketone is obtained by alcoholysis. Dipropionylethane (Octane-$\gamma\zeta$-dione), for example, is obtained by the following reactions (Compt. rend. **158**, 504).

$$(\cdot CH_2{\cdot}COCl)_2 + 2HOCMe_2{\cdot}COOH \longrightarrow (\cdot CH_2{\cdot}CO{\cdot}O{\cdot}CMe_2{\cdot}COOH)_2 \xrightarrow{PCl_5}$$

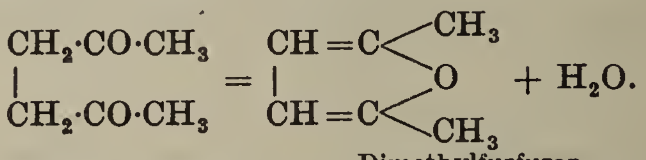


$$(\cdot CH_2{\cdot}CO{\cdot}O{\cdot}CMe_2{\cdot}COCl)_2 \xrightarrow{ZnEtI} \left(\cdot CH_2{\cdot}\underbrace{CEt{\cdot}O{\cdot}CMe_2{\cdot}CO}_{O}\right)_2 \longrightarrow (\cdot CH_2{\cdot}CO{\cdot}Et)_2$$

Further special methods for the preparation of individual diketones are described under the compounds concerned.

Reactions.—The 1 : 4-diketones are incapable of salt formation, and are consequently insoluble in alkalis. They readily form mono- and dioximes, and mono- and di-phenylhydrazones: the latter, unlike the osazones of the 1 : 2-diketones, are colourless. The most characteristic property of the 1 : 4-compounds is the readiness with which they form ring compounds derived from furan, thiophen and pyrrole (*Paal*, Ber. **18**, 58, 367, 2251).

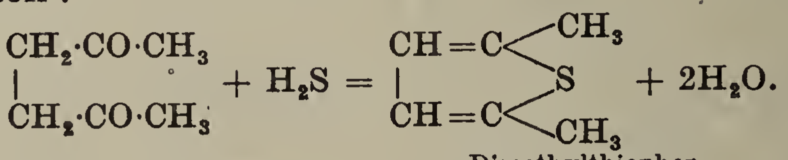
(1) The direct removal of one molecule of water from acetonylacetone by distillation with zinc chloride or P_2O_5 results in the formation of dimethylfurfuran (Ber. **20**, 1085):



Dimethylfurfuran.

Other γ-diketone compounds react in a similar manner (*Knorr*, Ber. **17**, 2756).

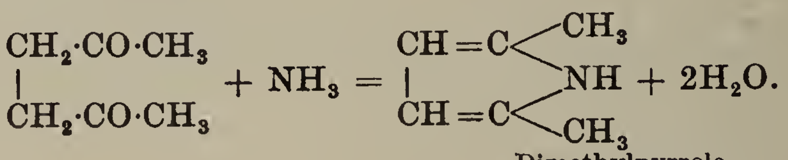
(2) When heated with phosphorus sulphide acetonylacetone yields dimethylthiophen:



Dimethylthiophen.

All the γ- diketones or 1 : 4-dicarboxyl compounds, *e.g.* the γ-ketonic acids (*q.v.*), yield the corresponding thiophen derivatives upon like treatment (Ber. **19**, 551).

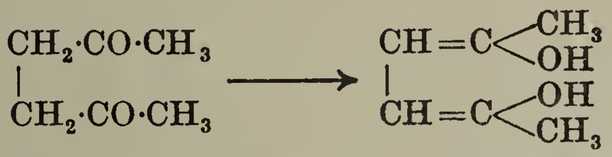
(3) Dimethylpyrrole is produced on heating acetonylacetone with alcoholic ammonia:



Dimethylpyrrole.

All compounds containing two CO-groups in the 1 : 4-position react similarly with ammonia and amines, *e.g.* diacetosuccinic ester and lævulinic ester. All the pyrrole derivatives formed as above, when boiled with dilute mineral acids, have the power of colouring a pine chip an intense red. This reaction is, therefore, a means of recognizing all 1 : 4-diketone compounds (Ber. **19**, 46).

In all these conversions of acetonylacetone into pyrrole, thiophen, and furfuran derivatives, it may be assumed that it first passes from the diketone form into the *pseudo*-form of the diolefine glycol (p. 50) :



$$\begin{array}{l} CH_2{\cdot}CO{\cdot}CH_3 \\ | \\ CH_2{\cdot}CO{\cdot}CH_3 \end{array} \longrightarrow \begin{array}{l} CH{=}C{<}^{CH_3}_{OH} \\ | \\ CH{=}C{<}^{OH}_{CH_3} \end{array}$$

and from this, by replacing the 2OH-groups with S, O, or NH, the corresponding furfuran, thiophen, and pyrrole compounds are produced (Ber. **19**, 551).

Acetonylacetone, sym.-*diacetylethane, βε-hexane-dione,* $CH_3CO{\cdot}CH_2CH_2{\cdot}COCH_3$, m.p. −9°, b.p. 194°, $D_{20} = 0{\cdot}973$, is obtained from pyrotritaric acid, $C_7H_8O_3$ (*q.v.*) ; from acetonylacetoacetic ester (*q.v.*), when heated to 160° with water (Ber. **18**, 58) ; and from *iso*pyrotritaric acid and diacetylsuccinic ester, when they are boiled with potassium carbonate solution (Ber. **33**, 1219). It is a liquid with an agreeable odour, and is miscible with water, alcohol, and ether.

β-Methylheptane-γζ-dione, *ω-dimethyllævulinic methyl ketone,* $CHMe_2{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3$, b.p. 91°/12 mm., is a degradation product of the terpene ketone, *tanacetone* (Vol. II). It is prepared from the glycol $Me_2C(OH){\cdot}CH(OH){\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3$ by boiling with dilute sulphuric acid (Ber. **35**, 1179).

Octane-γζ-dione, *dipropionylethane,* $C_2H_5{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}C_2H_5$, m.p. 34–35°, b.p. 98°/14 mm. (Compt. rend. **158**, 504).

(4) 1 : 5-, 1 : 6- and 1 : 7-Diketones

δ or **1 : 5-Diketones** are only obtained with difficulty. If it is attempted to prepare them from the δ-diketonedicarboxylic esters, resulting from the condensation of aldehydes and acetoacetic esters, *e.g.* αα-diacetylglutaric ester :

$$\begin{array}{r} CH_3CO \\ C_2H_5OCO \end{array}{>}CHCH_2CH{<}\begin{array}{l} COCH_3 \\ COOC_2H_5 \end{array}$$

by splitting off carboxyethyl groups, there results instead of, for example, βζ-heptane-dione, $CH_3CO{\cdot}CH_2CH_2CH_2{\cdot}COCH_3$, a cyclic compound,—3-methyl-Δ^2-*cyclo*hexen-1-one (Ann. **288**, 321).

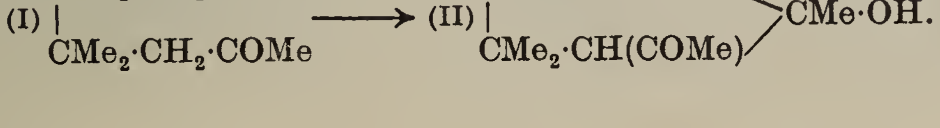
Heptane-βζ-dione, $CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}CO{\cdot}CH_3$, m.p. 34°, b.p. 96–97°/10 mm., is however obtained by decomposition of the ozonide of α-*iso*caoutchouc (Ber. **47**, 784). *Dioxime,* m.p. 87°. It changes to the methyl*cyclo*hexenone when warmed with dilute sodium hydroxide.

1 : 6- or **ε-Diketones.** *αδ-Diacetylbutane, βη-octane-dione,* m.p. 44°, results from the electrolysis of potassium lævulinate :

$$2CH_3COCH_2CH_2 \vdots COO \vdots K \longrightarrow CH_3COCH_2CH_2{\cdot}CH_2CH_2{\cdot}COCH_3.$$

It is also obtained by the ketonic decomposition of diacetyladipic ester (*q.v.*) (Ber. **33**, 650).

The compound *δδεε-tetramethyloctane-βη-dione,* (I) passes immediately on formation into the isomeric acetylpentamethyl*cyclo*pentanol (II) and there is no tendency for the reverse change to occur. The compound only yields a *monoxime* and a *monosemicarbazone,* both of which occur in two stereoisomeric forms, but no di- derivative could be obtained (J.C.S. **1927**, 594).



$$\text{(I)} \begin{array}{l} CMe_2{\cdot}CH_2{\cdot}COMe \\ | \\ CMe_2{\cdot}CH_2{\cdot}COMe \end{array} \longrightarrow \text{(II)} \begin{array}{l} CMe_2 \text{——} CH_2 \\ | \\ CMe_2{\cdot}CH(COMe) \end{array}{>}CMe{\cdot}OH.$$

1 : 7- or ζ-**Diketone**, *diacetylpentane*, $CH_3CO{\cdot}(CH_2)_5{\cdot}COCH_3$, belongs to this class. When reduced, it undergoes an intramolecular pinacone formation and becomes dimethyl*cyclo*heptanediol, $CH_3{\cdot}\overbrace{C(OH)[CH_2]_5C}(OH)CH_3$ (Ber., **23**, R. 249 : **24**, R. 634 : **26**, R. 316).

NITROGEN-CONTAINING DERIVATIVES OF THE DIALDEHYDES, ALDEHYDE KETONES AND DIKETONES

1. For the action of **ammonia** on glyoxal and acetonylacetone, see pp. 401, 404. Action of ammonia on acetylacetone, see p. 397.

2. *Oximes*

A. **Monoximes.**—(*a*) *Aldoximes of the α-aldehyde ketones and monoximes of the α-diketones :* iso*nitrosoketones.* These bodies are formed (1*a*) by the action of nitrogen trioxide on ketones (Ber. **20**, 639). By this reaction mixed ketones, which contain the —CO— group united to two CH_2-groups, yield two different *iso*nitroso-ketones ; but if the —CO— group is joined to a tertiary alkyl, only one *iso*nitroso-ketone is formed (C. 1898, II. 965).

(1*b*) When amyl nitrite in the presence of sodium ethoxide or hydrochloric acid acts on ketones (Ber. **20**, 2194 : **28**, 1915) :

$$CH_3COCH_3 + NO{\cdot}O{\cdot}C_5H_{11} = CH_3COCH(:N{\cdot}OH) + C_5H_{11}{\cdot}OH.$$

An excess of amyl nitrite decomposes the oximino-body, whereby the oximino-group is replaced by oxygen, with the production of α-diketo-derivatives (Ber. **22**, 527 : C. 1904, II. 1701).

(2) As acetone is formed from acetoacetic ester, *iso*nitroso- or oximino-acetone can be prepared from the oximino-derivative of acetoacetic ester (Ber. **15**, 1326). Nitrous acid decomposes acetoacetic acid into oximino-acetone and carbon dioxide :

$$CH_3COCH_2CO_2H + NO{\cdot}OH = CH_3{\cdot}COCH(:N{\cdot}OH) + CO_2 + H_2O.$$

Similarly, by the action of nitrous acid, nitrosyl sulphate or chloride, the oximinol compounds of the higher acetones can be directly derived from the monoalkyacetoacetic acids and their esters by elimination of carbon dioxide (Ber. **20**, 531 : C. 1904, II. 1700) :

$$CH_3COCH{<}\begin{smallmatrix}R\\CO_2H\end{smallmatrix} + NO{\cdot}OH = CH_3COC{\leqslant}\begin{smallmatrix}R\\N{\cdot}OH\end{smallmatrix} + CO_2 + H_2O,$$

whilst the dialkylacetoacetic acids do not react (Ber. **15**, 3067).

Properties.—The *iso*nitroso-ketones are colourless, crystalline bodies, easily soluble in alcohol, ether and chloroform, but usually more sparingly soluble in water. They dissolve in the alkalis, the hydrogen of the hydroxyl group being replaced by metal, with the formation of salts having an intensely yellow colour. They yield a yellow coloration with phenol and sulphuric acid, and not the blue coloration of the nitroso-reaction (Ber. **15**, 1529).

Reactions.—(1) The oximino-group can be split off and be replaced by oxygen, which will lead to the formation of diketo-bodies, —CO·CO—. This result may be brought about by the addition of sodium bisulphite and boiling the resulting imidosulphonic acid with dilute acids (Ber. **20**, 3162). The reaction also takes place when *iso*nitrosoketones are boiled directly with dilute sulphuric acid (Ber. **20**, 3213). The decomposition is sometimes more readily effected by nitrous acid (Ber. **22**, 532 : C. 1904, II. 1701).

(2) The aldoximino-ketones, like the aldoximes (p. 250), are converted by dehydrating agents—*e.g.* acetic anhydride—into acyl cyanides or α-ketocarboxylic nitriles (*q.v.*) (Ber. **20**, 2196).

(3) Aminoketones (p. 397) are produced in the reduction of *iso*nitroso-ketones by means of stannous chloride.

(4) Two molecules of phenylhydrazine, acting on the *iso*nitroso-ketones, produce *osazones*, *e.g.* $CH_3{\cdot}C(N_2H{\cdot}C_6H_5)CH(N_2H{\cdot}C_6H_5)$—acetonosazone (Ber. **22**, 528). Semicarbazide gives rise to *semicarbazone oximes*, most of which are slightly soluble and possessed of high melting points (C. 1904, II. 304, 1700).

(5) By the further action of hydroxylamine or its hydrochloride (Ber. **16**, 182 : C. 1904, II. 1700) on *iso*nitroso-ketones, *dioximes* of the α-aldehyde ketones and α-diketones are produced.

(6) Halogen alkyls acting on the salts of *iso*nitroso-ketones produce ethers (comp. Ber. **15**, 3073 : **38**, 1917):

$$CH_3CO{\cdot}C(NOK)CH_3 + CH_3I = CH_3CO{\cdot}C(NOCH_3){\cdot}CH_3 + KI.$$

which are the alkoximes of the α-diketones. They are more stable than the free *iso*nitroso-ketones, and are therefore more suitable for use in many synthetic reactions.

*iso***Nitroso-acetone,** *aldoxime of pyroracemic aldehyde,* $CH_3{\cdot}CO{\cdot}CH : N{\cdot}OH$, m.p. 65°, is very readily soluble in water; crystallizes in silvery, glistening tablets or prisms; melts and decomposes at higher temperatures, but may be volatilized in a current of steam.

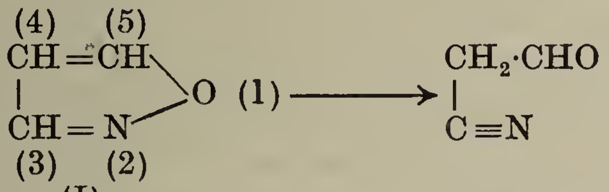
Monoximes of the α-Diketones.—iso*Nitroso-ethyl methyl ketone,* $CH_3CO{\cdot}C{=}NOH{\cdot}CH_3$, m.p. 74°, b.p. 185–188°. Preparation (Ber. **35**, 3290). Action of HCl on *iso*nitroso-ethyl methyl ketone (Ber. **38**, 3357). iso*Nitroso-methyl propyl ketone,* $CH_3CO{\cdot}C{=}NOH{\cdot}CH_2CH_3$, m.p. 52–53°, b.p. 183–187°. iso*Nitroso-diethyl ketone,* $C_2H_5{\cdot}COC{=}NOH{\cdot}CH_3$, m.p. 59–62°. iso*Nitroso-methyl butyl ketone,* $CH_3{\cdot}COC{=}NOH{\cdot}C_3H_7$, m.p. 49·5°. iso*Nitroso-methyl* iso*butyl ketone,* $CH_3{\cdot}COC{=}NOH{\cdot}CH(CH_3)_2$, m.p. 75°. iso*Nitroso-methyl* iso*amyl ketone,* $CH_3{\cdot}$, $COC{=}NOH{\cdot}CH_2{\cdot}CH(CH_3)_2$, m.p. 42° C. iso*Nitroso-methyl* iso*capryl ketone,* $CH_3{\cdot}COC{=}NOH{\cdot}CH_2CH_2CH(CH_3)_2$, m.p. 38°.

For other *iso*nitroso-ketones see C. 1899, I. 190 : II. 524 : 1904, II. 1700.

B. Oxime-anhydrides of the β-Diketones or Isoxazoles.

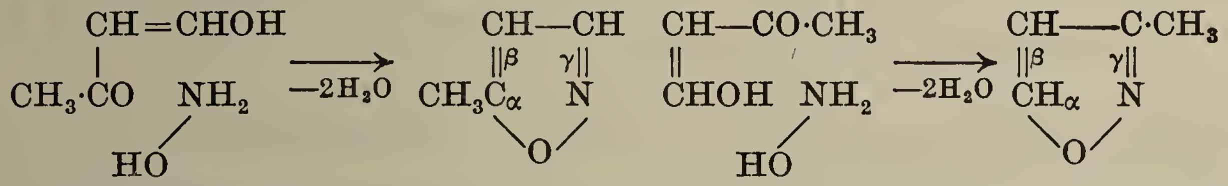
Monoximes of the β-formylketones and of the β-diketones are not known. In the attempt to prepare them water is lost and an intramolecular anhydride formation takes place. The oxime-anhydrides are isomeric with oxazoles, which also consist of five members; hence their name, *isoxazoles* (Ber. **21**, 2178 : **24**, 390 : **25**, 1787).

Isoxazole, *oxime-anhydride of malonic dialdehyde,* (see Formula (I) below) b.p. 95°, is prepared from propargyl aldehyde or β-anilino-acrolein anil (p. 399) by hydroxylamine. Alcoholic alkalis convert it into cyanacetaldehyde (p. 457) (Ber. **36**, 3665):



(I)

5-*Methylisoxazole,* $CH_3C_3H_2NO$, b.p. 122°, and 3-methylisoxazole, $CH_3C_3H_2NO$, b.p. 118°, result from hydroxymethylene acetone. They are transparent liquids, having an intense odour resembling that of pyridine. 5-Methylisoxazole readily becomes rearranged into cyanacetone (p. 475):



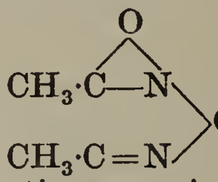
3 : 5-*Dimethylisoxazole,* b.p. 141°, has a very peculiar odour, and is obtained from acetylacetone and hydroxylamine hydrochloride.

C. Dioximes.

(*a*) **α-Dioximes.**—When glyoxal, of which the monoxime is not known, pyroracemic aldehyde and the α-diketones are treated with hydroxylamine hydrochloride, the α-*dioximes* or *glyoximes* are formed. They can also be obtained from α-*iso*nitroso-ketones or α-dichloroketones. The glyoximes form characteristic complex compounds with Ni, Co, Pt, Fe, Cu, which are stable and strongly coloured; the metal is united to two glyoxime molecules (Ber. **39**, 2692, 3382).

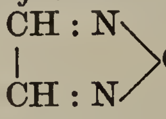
Glyoxime, $CH(:NOH){\cdot}CH(:NOH)$, m.p. 178° (Ber. **17**, 2001 : **25**, 705 : **28**, R. 620), is prepared from trichlorolactic acid (p. 421). *Methylglyoxime, acetoximic acid,* $CH_3C(NOH){\cdot}CH(NOH)$, m.p. 153°. Dimethylglyoxime, *diacetyldioxime,* $CH_3C(NOH){\cdot}C(NOH)CH_3$, m.p. 234° (Ber. **28**, R. 1006 : J. pr. Chem. [2] **77**, 414) is employed as a sensitive test for the presence of nickel. *Methylethylglyoxime,* $CH_3C(NOH){\cdot}C(NOH){\cdot}C_2H_5$, m.p. 172° (Ber. **34**, 3978). *Methylpropylglyoxime,* m.p. 168°. tert.-*Butylglyoxime,* $(CH_3)_3C{\cdot}C(NOH)CH(NOH)$, m.p. 102°, is prepared from dichloropinacolin. *Methylisobutylglyoxime*, m.p. 170–172°. Higher homologues of glyoxime, see C. 1899, II. 524 : 1904, II. 1700.

(*b*) **Furoxan derivatives** (Ber. **23**, 3496) result when NO_2 acts on an ethereal solution of the glyoximes : *dimethyl furoxan*, b.p. 222°.

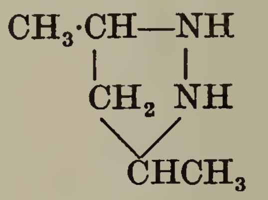


Methylethylfuroxan, b.p. 115°/16 mm. (Constitution, see Ann. **424**, 107).

(*c*) **Furazans**, *azoxazoles*, *furodiazoles* are the anhydrides obtained from certain α-dioximes. *Furazan*, itself is not known, whilst dimethylfurazan, for example, has been prepared from diacetyl dioxime.



(*d*) **β-Dioximes**, *acetylacetone dioxime*, $CH_3C(NOH)CH_2C(NOH)CH_3$, m.p. 150°, is produced from acetylacetone by an excess of hydroxylamine. It easily gives this up and is converted into dimethylisoxazole (see above). Reduction by sodium and alcohol gives βδ-diaminopentane. Electrolytic reduction in sulphuric acid solution leads to the formation of dimethylpyrazolidine,



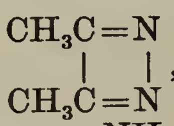
(Ber. **36**, 219).

(*e*) **γ-Dioximes**, derived from the γ-dialdehydes, γ-aldehyde-ketones and γ-diketones, may be prepared (1) by the action of hydroxylamine on pyrrole (Ber. **22**, 1968) and alkylpyrroles (Ber. **23**, 1788) ; (2) from γ-diketones and hydroxylamine. They are decomposed by boiling alkalis into the corresponding acids, or γ-diketones ; the latter are far better obtained by means of nitrous acid.

Succinaldehyde dioxime, HON : $CHCH_2CH_2CH$: NOH, m.p. 173°, passes upon reduction into tetramethylene diamine (p. 384), and into succinic dialdehyde by the action of N_2O_3 (Ber. **35**, 1184). *Ethylsuccinaldioxime*, HON : $CHCH(C_2H_5)$-CH_2CH : N(OH), m.p. 135°. *Propionylpropionaldioxime*, CH_3CH_2C : $N(OH)CH_2$-CH_2CH : N(OH), m.p. 85°. *Methyllævulinaldioxime*, CH_3C : $N(OH)CH_2CH(CH)_3$-CH : N(OH). *Acetonylacetone dioxime*, CH_3C : $N(OH)CH_2CH_2C$: $N(OH)CH_3$, m.p. 135°. *ωω-Diacetylpentane dioxime*, CH_3C : $N(OH)[CH_2]_5C$: $N(OH)CH_3$, m.p. 172°.

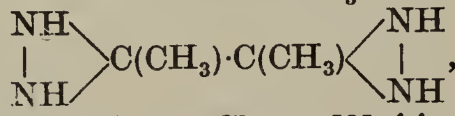
3. *Hydrazine, Phenylhydrazine and Semicarbazide Derivatives*

Dimethylaziethane,



$$\begin{array}{l} CH_3C{=}N \\ \quad | \quad\;\; | \\ CH_3C{=}N \end{array}$$

, m.p. above 270°, and *dimethylbishydrazimethylene*,

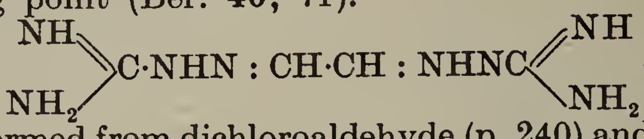


, m.p. 158°, are obtained from diacetyl and hydrazine (J. pr. Chem. [2] **44**, 174). Dimethylaziethane is also prepared from *diacetyl acetylhydrazone*, $CH_3C(N : N{\cdot}COCH_3)$: $C(OH)CH_3$, m.p. 167°, by heating it with alkalis.

The **mono-semicarbazones** of the α-diketones dissolve in alkalis, like the monoximes (p. 406), to a yellow solution. *Diacetyl semicarbazone*, CH_3COC-$(NNHCONH_2)CH_3$, or CH_2 : $C(OH){\cdot}C(NNHCONH_2)CH_3$, m.p. 235°. Acetyl propionyl semicarbazone, m.p. 209° (Ber. **36**, 3183°).

Glyoxal disemicarbazone, $(NH_2CONHN : CH\text{—})_2$, is a slightly soluble crystalline powder of high melting point (Ber. **40**, 71).

Glyoxal bisguanidine,

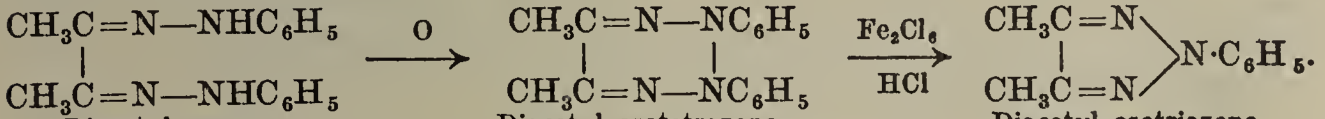


$+H_2O$, m.p. 265°, with decomposition, is formed from dichloroaldehyde (p. 240) and aminoguanidine (Ann. **202**, 284). *Diacetyl disemicarbazone*, m.p. 279°.

Monophenylhydrazones.—*Hydrazone of pyroracemic aldehyde*, $CH_3CO{\cdot}CH$:-$N{\cdot}NH{\cdot}C_6H_5$, m.p. 148°, is obtained by hydrolysing the reaction-product resulting from diazobenzene chloride and sodium acetoacetic ester with alcoholic sodium hydroxide (C. 1901, I. 299). *Diacetylphenylhydrazone*, $CH_3CO{\cdot}C:(NNHC_6H_5){\cdot}CH_3$, m.p. 133°, has been prepared from diacetyl and from methyl-acetoacetic ester (*Japp* and *Klingemann*) (Ann. **247**, 190).

α-Acetylpropionylphenylhydrazone, $CH_3C(:NNHC_6H_5){\cdot}COC_2H_5$, m.p. 97°, is obtained from acetyl propionyl. *β-Acetylpropionylphenylhydrazone*, $CH_3CO{\cdot}C:(NNHC_6H_5)C_2H_5$, m.p. 117°, is prepared from ethylacetoacetic acid and diazobenzene chloride.

Diphenylhydrazones or Osazones.—Glyoxal (p. 398), methyl glyoxal (p. 400), the α-diketones and the α-*iso*nitroso-ketones, when treated with phenylhydrazine, lose two molecules of water or water and hydroxylamine, respectively, and form diphenylhydrazones or *osazones*, which can also be obtained from α-hydroxyaldehydes, α-hydroxyketones, α-aminoaldehydes and α-aminoketones, the alcohol or other group adjacent to the keto group undergoing oxidation. The osazones are especially important in the chemistry of the aldopentoses, and the aldo- and ketohexoses. The osazones are oxidized by potassium chromate and acetic acid to *osotetrazones*, which are converted by hydrochloric acid and ferric chloride into *osotriazones*:



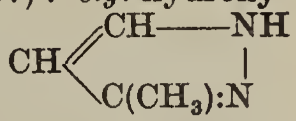
Diacetyl osazone. Diacetyl osotetrazone. Diacetyl osotriazone.

Glyoxal osazone, $C_6H_5NH{\cdot}N:CHCH:N{\cdot}NHC_6H_5$, m.p. 177°, is also formed from formaldehyde and phenylhydrazine, with the intermediate formation of glycolyl aldehyde (p. 387) (Ber. **30**, 2459). *Glyoxal osotetrazone*, m.p. 145° (Ber. **17**, 2001: **21**, 2752: **26**, 1045).

Methylglyoxal osazone, m.p. 145° (Ber. **26**, 2203). *Methylglyoxal osotetrazone*, m.p. 107°. *Methylglyoxal osotriazone*, b.p. 150°/10 mm. (Ber. **21**, 2755).

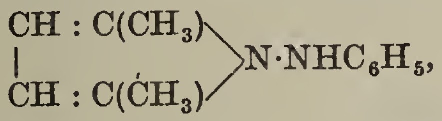
Diacetyl osazone, m.p. 236° (decomp.) (Ber. **20**, 3184; Ann. **249**, 203). *Diacetyl osotetrazone*, m.p. 169° (decomp.). *Diacetyl osotriazone*, m.p. 35°, b.p. 255° (Ber. **21**, 2759). *Acetylpropionyl osazone*, m.p. 162° (Ber. **21**, 1414: Ann. **247**, 221).

The 1 : 3-diketones and the 1 : 3-hydroxymethylene ketones (p. 396) unite with hydrazine and phenylhydrazine, forming *pyrazoles* (Vol. III), which may be regarded as derivatives of the 1 : 3-olefine ketols (Ann. **279**, 237): *e.g.* hydroxymethylene acetone and hydrazine yield 3-*methylpyrazole*,



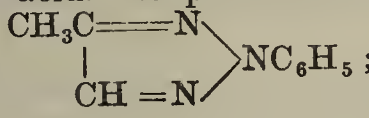
(Ber. **27**, 954).

Acetonylacetone, a 1 : 4-diketone, and phenylhydrazine yield: *Acetonylacetone diphenylhydrazone*, m.p. 120°, and *anilino-dimethyl-pyrrole*,



m.p. 90°, b.p. 270° (Ber. **18**, 60: **22**, 170). (Products from acetylacetone and hydrazine).

α-Hydrazoximes.—*Methylglyoxal phenylhydrazoxime*, $CH_3{\cdot}C:N(NHC_6H_5){\cdot}CH:NOH$, m.p. 134°, is prepared by the action of phenylhydrazine on *iso*-nitroso-acetoacetic acid. It parts readily with water and yields methyl-*N*-phenyl-osotriazole,



(Vol. III) (Ann. **262**, 278).

HYDROXY-ACIDS AND THEIR DERIVATIVES

7. HYDROXY-ACIDS, $C_nH_{2n}(OH)\cdot COOH$

The acids of this series show simultaneously the reactions of an alcohol and a carboxylic acid. The reactions of any individual member of the series are conditioned by two factors, (i) the nature of the alcoholic hydroxy group, which may be primary, secondary or tertiary, and which yields different oxidation products in each of the three cases, and (ii) the relative positions of the hydroxy and carboxyl groups in the molecule.

The " Geneva names " are formed by the insertion of the syllable " ol," characteristic of alcohols, between the name of the hydrocarbon and the word " acid " ; $CH_2OH\cdot COOH$, hydroxyacetic acid, or [ethanol acid].

Glycollic and lactic acids are the best-known and most important representatives.

General Methods of Formation

(1) Careful oxidation (*a*) of glycols containing at least one primary alcohol group with dilute nitric acid, or platinum sponge and air, *e.g.* :

$$CH_2OH\cdot CH_2OH + O_2 \longrightarrow CH_2OH\cdot COOH + H_2O.$$

(*b*) The oxidation of hydroxyaldehydes.

(2) The reduction of the aldehyde acids, the ketonic acids, and dicarboxylic acids by sodium amalgam, zinc and hydrochloric or sulphuric acid, sodium and alcohol, or electrolysis.

Pyroracemic acid, $CH_3\cdot CO\cdot CO_2H + 2H = CH_3\cdot CH(OH)\cdot CO_2H.$
Oxalic acid, $COOH\cdot COOH + 4H = COOH\cdot CH_2OH + H_2O.$

This reaction is frequently used in preparing β-, γ- and δ-hydroxy-acids from β-, γ- and δ-ketone carboxylic esters.

(3) Fatty acids containing a tertiary hydrogen atom can be directly oxidized to the hydroxy-acid by permanganate or nitric acid (*R. Meyer*, Ber. **11**, 1283, 1787 : **12**, 2238 : Ann. **208**, 60 : **220**, 56 : Ber. **14**, 1782 : **16**, 2318).

(4) By heating unsaturated fatty acids with aqueous potassium or sodium hydroxide to 100° (Ann. **283**, 50).

(5) By the reaction of the monohalogen fatty acids with silver oxide, boiling alkalis, or even water. The conditions of the reaction are perfectly similar to those observed in the conversion of the alkyl halides into alcohols.

$$CH_2Cl\cdot CO_2H + H_2O = CH_2(OH)COOH + HCl.$$

The α-derivatives yield α-hydroxy-acids ; the β-derivatives are occasionally changed to unsaturated acids by the splitting-off of a halogen acid, whilst the γ-compounds form γ-hydroxy-acids, which subsequently pass into lactones. γ-Halogen acids are converted directly into lactones by the alkali carbonates.

(6) By the action of nitrous acid on amino-acids:

$$\underset{\text{Aminoacetic acid.}}{CH_2(NH_2)\cdot CO_2H} + HNO_2 = \underset{\text{Hydroxyacetic acid.}}{CH_2(OH)\cdot CO_2H} + N_2 + H_2O.$$

(7) The hydroxy-acids can be obtained from the diazo-fatty acids on boiling them with water or dilute acids.

(8) From the α-ketone-alcohols—*e.g.* butyroin and *iso*valeroin (p. 394)—on treating them with alkalis and air, the first-formed 1 : 2 diketone undergoing a benzilic acid transformation (Ann. 434, 271).

Nucleus-synthetic Methods of Formation.—(9) By allowing hydrocyanic acid and hydrochloric acid to act on the aldehydes and ketones. At first *cyanohydrins*, the nitriles of hydroxy-acids (*q.v.*), are produced after which hydrochloric acid changes the cyanogen group into carboxyl:

$$1.\ CH_3\cdot CHO + HNC = CH_3\cdot CH(OH)\cdot CN$$
$$2.\ CH_3\cdot CH(OH)\cdot CN + 2H_2O = \underset{\alpha\text{-Hydroxypropionic acid.}}{CH_3\cdot CH(OH)\cdot COOH} + NH_3.$$

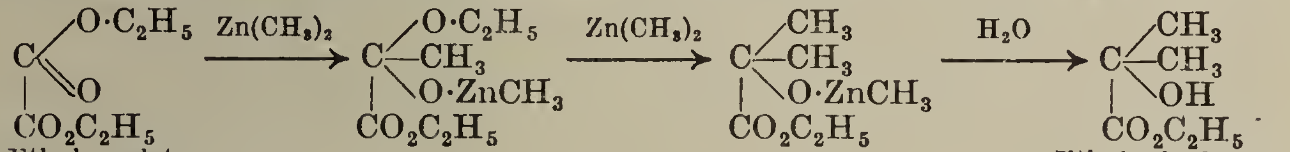
The conversion of the cyanohydrins into the hydroxy acids is carried out by means of concentrated hydrochloric acid, the amides being produced in the cold, and converted into the acids on heating with dilute hydrochloric acid. Dilute sulphuric acid sometimes acts more readily.

Ethylene oxide reacts with hydrogen cyanide like acetaldehyde.

(10) The glycol chlorohydrins (p. 369) undergo a similar alteration through the action of potassium cyanide and acids:

$$1.\ CH_2(OH)\cdot CH_2Cl + KNC = CH_2(OH)CH_2\cdot CN + KCl,$$
$$2.\ CH_2(OH)\cdot CH_2CN + 2H_2O = \underset{\beta\text{-Hydroxypropionic acid.}}{CH_2(OH)\cdot CH_2\cdot CO_2H} + NH_3.$$

(11) A method of ready applicability in the synthesis of α-hydroxy-acids consists in acting on ethyl oxalate with zinc and alkyl iodides (*Frankland* and *Duppa*). This reaction is like that in the formation of tertiary alcohols from the acid chlorides by means of zinc ethyl, or of the secondary alcohols from alkyl formates (p. 132)—1 and 2 alkyl groups are introduced into one carboxyl group (Ann. 185, 184):



Ethyl oxalate. Ethyl α-hydroxy-*iso*butyrate.

If we employ two alkyl iodides, two different alkyl groups may be introduced.

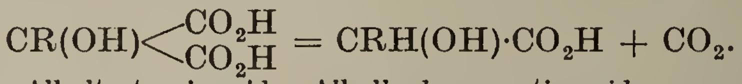
(12*a*) β-Hydroxy-acids are formed when aldehydes or ketones are condensed with α-halogen fatty acid esters by means of zinc or magnesium; *e.g.* propionic aldehyde and α-bromopropionic ester yield α-methyl-β-ethylhydracrylic acid, $C_2H_5CH(OH)CH(CH_3)COOH$; trioxymethylene, α-bromo*iso*butyric ester and zinc yield αα-dimethylhydracrylic acid (comp. p. 423) (C. 1901, I. 1196: II. 30: 1902, I. 856).

(12*b*) Ketone acid esters and magnesium alkyl iodides produce, in part, tertiary hydroxy-acid esters; also, ethyl oxalyl chloride with magnesium alkyl halides yields the ethyl oxalyl derivative of the α-hydroxy-acid ester (C. 1902, II. 1359: 1900, II. 1110):

$$CH_3COCO_2C_2H_5 + CH_3MgI = (CH_3)_2C(OMgI)CO_2C_2H_5$$
$$2C_2H_5OCO\cdot COCl + 2CH_3MgI = C_2H_5OCO\cdot C(CH_3)_2O\cdot CO\cdot CO_2C_2H_5 + 2MgClI.$$

(13) When sodium or sodium ethoxide acts on the acetic esters and propionic esters it converts them into β-ketone-carboxylic esters, but in the case of butyric and *iso*butyric esters it produces the ether esters of β-hydroxy-acids, such as ethoxycaprylic ester, $(CH_3)_2CH\cdot CH(OC_2H_5)\cdot C(CH_3)_2CO_2C_2H_5$, from *iso*butyric ester (Ann. **249**, 54).

Cleavage-Reactions.—(14) The fatty acids are formed from alkyl malonic acids, $CRR'(CO_2R)_2$, by the withdrawal of a carboxyl group (p. 545), and the hydroxy-fatty acids are obtained in a similar manner from alkyl hydroxymalonic acids or tartronic acids:



$$CR(OH)\Big\langle{}^{CO_2H}_{CO_2H} = CRH(OH)\cdot CO_2H + CO_2.$$

Alkyltartronic acid. Alkylhydroxyacetic acid.

Isomerism.—The possible cases of isomerism with the hydroxy-acids are most simply deduced by considering the hydroxy-acids as the mono-hydroxyl substitution products of the fatty acids. Then the isomers are the same as the mono-halogen fatty acids, which may be regarded as the haloid esters of the alcoholic acids corresponding with them.

Hydroxyacetic or glycollic acid is the only acid which can be obtained from acetic acid:

$CH_3\cdot COOH$	$CH_2OH\cdot COOH$
Acetic acid.	Glycollic acid (p. 414)

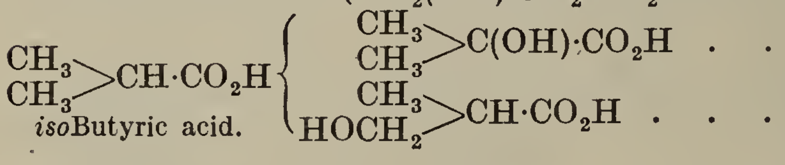
Propionic acid yields two hydroxypropionic acids:

$CH_3CH_2\cdot COOH$	$CH_3\overset{*}{C}H(OH)\cdot COOH$	$CH_2(OH)CH_2\cdot COOH$
Propionic acid.	α-Hydroxypropionic acid. Lactic acid (p. 415).	β-Hydroxypropionic acid. Hydracrylic acid (p. 422).

These are distinguished as α- and β-hydroxypropionic acids respectively. The α-acid contains an asymmetric carbon atom, and therefore, theoretically, should yield an inactive variety, which can be resolved, and two optically active modifications: all three forms are known.

Normal butyric acid yields three and *iso*butyric acid two mono-hydroxy-acids:

$$\underset{n\text{-Butyric acid.}}{CH_3\cdot CH_2\cdot CH_2CO_2H}\begin{cases} CH_3\cdot CH_2\cdot CH(OH)\cdot CO_2H & \alpha\text{-Hydroxybutyric acid (p. 418)} \\ CH_3\cdot CH(OH)\cdot CH_2\cdot CO_2H & \beta\text{-Hydroxybutyric acid (p. 423)} \\ CH_2(OH)\cdot CH_2\cdot CH_2\cdot COOH & \gamma\text{-Hydroxybutyric acid (p. 427)} \end{cases}$$



$$\underset{iso\text{Butyric acid.}}{{}^{CH_3}_{CH_3}\!\!>CH\cdot CO_2H}\begin{cases} {}^{CH_3}_{CH_3}\!\!>C(OH)\cdot CO_2H \quad . \quad . & \alpha\text{-Hydroxy}iso\text{butyric acid (p. 418)} \\ {}^{CH_3}_{HOCH_2}\!\!>CH\cdot CO_2H \quad . \quad . \quad . & \beta\text{-Hydroxy}iso\text{butyric acid (p. 423).} \end{cases}$$

Properties and Reactions

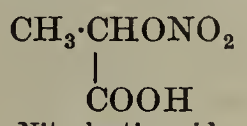
Properties.—The hydroxy-fatty acids containing one OH-group are more readily soluble in water, and less soluble in ether than the parent acids (p. 296). They are less volatile and, as a general rule, cannot be distilled without decomposition.

Reactions.—(1) The alcohol-acids behave like the monocarboxylic acids in that they yield, through a change in the carboxyl group, normal salts, esters, amides, and nitriles and other derivatives:

$$CH_2OH\cdot COOK \qquad CH_2OH\cdot COOC_2H_5 \qquad CH_2OH\cdot CONH_2 \qquad CH_2OH\cdot CN.$$

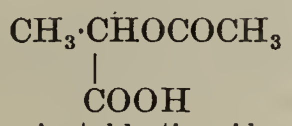
(2) The remaining OH-group behaves like that of the alcohols, of which the hydrogen may be replaced by alkali metals and alkyls;

by acid radicals such as NO_2, by the action of a mixture of concentrated nitric and sulphuric acids; or by a carboxylic acid residue, by the action of acid chlorides and anhydrides, such as the acetyl residue by means of acetyl chloride and anhydride,



$$\begin{array}{l} CH_3\cdot CHONO_2 \\ \quad | \\ COOH \end{array}$$

Nitrolactic acid.



$$\begin{array}{l} CH_3\cdot CHOCOCH_3 \\ \quad | \\ COOH \end{array}$$

Acetyl lactic acid.

Both of these reactions are characteristic of alcoholic hydroxyl groups.

Similarly, ethers can be formed from the alcoholic hydroxyl group. Thus, the compounds ethoxyacetic acid (ethylglycollic acid) and its ester are known. Alkalis remove the alkyl *ester*-group, leaving the *ether*-group untouched. Thus, ethyl ethoxyacetate is hydrolysed to ethoxyacetic acid.

$$\underset{\text{Ethyl ethoxyacetate.}}{C_2H_5O\cdot CH_2\cdot COOC_2H_5} \longrightarrow \underset{\substack{\text{Ethoxyacetic acid.} \\ \text{(Ethylglycollic acid).}}}{C_2H_5O\cdot CH_2\cdot COOH}$$

(3) PCl_5 replaces the two hydroxyl groups by chlorine:

$$\underset{\text{Glycollic acid.}}{CH_2OH\cdot COOH} + 2PCl_5 \longrightarrow \underset{\text{Chloroacetyl chloride.}}{CH_2Cl\cdot COCl} + 2POCl_3 + 2HCl.$$

The acid chlorides corresponding with the hydroxy-acids are not known. Instead of these we get the chlorides of the corresponding monochloro-fatty acids, in which the chlorine in union with CO is very reactive with water and alcohols, yielding free acids and their esters; in the case cited, monochloroacetic acid, $CH_2Cl\cdot CO_2H$, and its esters result. The remaining chlorine atom is, on the contrary, more firmly united, as in chloroethane.

(4) The hydroxy-acids are reduced to their corresponding fatty acids (p. 296) when they are heated with hydriodic acid.

(5) Whilst in the preceding transpositions all the hydroxy-acids react similarly, the primary, secondary and tertiary alcohol-acids show marked differences when they are oxidized.

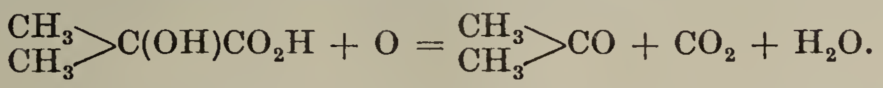
(*a*) The *primary* hydroxy-acids yield, by oxidation, aldehyde acids and dicarboxylic acids.

$$\underset{\text{Glycollic acid.}}{CH_2OH\cdot COOH} \longrightarrow \underset{\text{Glyoxylic acid.}}{CHO\cdot COOH} \longrightarrow \underset{\text{Oxalic acid.}}{COOH\cdot COOH}$$

(*b*) The *secondary* hydroxy-acids yield ketone acids: the α-ketonic acids change to aldehydes and CO_2, the β-ketonic acids to ketones and CO_2:

$$CH_3CH(OH)\cdot COOH \longrightarrow CH_3CO\cdot COOH \longrightarrow CH_3CHO + CO_2.$$

(*c*) *Tertiary* α-hydroxy-acids yield ketones:



$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>C(OH)CO_2H + O = \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>CO + CO_2 + H_2O.$$

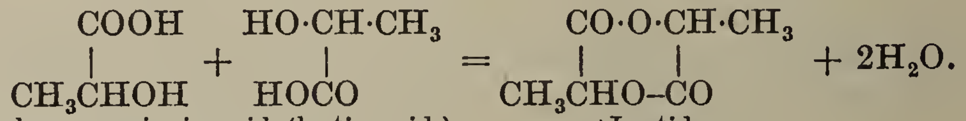
(6) The α-hydroxy-acids undergo a similar decomposition when heated with dilute sulphuric or hydrochloric acid or by action of concentrated H_2SO_4. Their carboxyl group is removed as formic acid (when concentrated H_2SO_4 is employed, CO and H_2O are the products):

$$(CH_3)_2C(OH)CO_2H = (CH_3)_2CO + HCO_2H.$$
$$CH_3CH(OH)CO_2H = CH_3\cdot CHO + HCO_2H,$$

Another reaction takes place simultaneously to a small extent: water is eliminated, and unsaturated acids are produced. This change is easily effected when PCl_3 is allowed to act on the esters of α-hydroxy-acids (p. 337).

(7) The behaviour of the α-, β-, γ-, or δ-hydroxy-acids on elimination of water from carboxyl and alcoholic hydroxyl groups is important.

(*a*) The *α-hydroxy-acids* lose water when they are heated and yield cyclic double esters—the *lactides*—in the formation of which two molecules of the α-hydroxy-acid have taken part:



$$\begin{array}{ccccc} COOH & & HO\cdot CH\cdot CH_3 & & CO\cdot O\cdot CH\cdot CH_3 \\ | & + & | & = & | \qquad | \\ CH_3CHOH & & HOCO & & CH_3CHO\text{–}CO \end{array} + 2H_2O.$$

α-Hydroxypropionic acid (lactic acid.) Lactide.

(*b*) When the *β-hydroxy-acids* are heated alone, water is withdrawn and unsaturated acids are the products (p. 337; C. 1897, I. 363):

$$CH_2(OH)\cdot CH_2CO_2H = CH_2 : CHCO_2H + H_2O.$$

β-Hydroxypropionic acid. Hydracrylic acid. Acrylic acid.

(*c*) The γ- and *δ-hydroxy-acids* lose water at the ordinary temperature, and change more or less completely into simple cyclic esters—the γ- and *δ-lactones*. The internal anhydrides of the β-hydroxy-acids, the β-lactones, are very much more difficult to prepare and much less stable (p. 271).

The α-, β-, γ- and δ-amino acids show the same differences in behaviour as the corresponding hydroxy-acids.

Structure of Normal Carbon Chains and the Formation of Lactones

The peculiar differences in the behaviour of the α-, β-, γ- and δ-hydroxy-acids when they split off water have contributed to the development of a representation of the spacial arrangement or configuration of carbon chains (Ber. **15**, 630). The assumption that the atoms of a molecule not linked to each other in a formula can exert an affinity upon one another has led to the idea that, in a union of more than two C atoms, these atoms arrange themselves, not in a straight line, but upon a curve. We can then comprehend that cyclic, simple ester formation can not take place between the first and second carbon atoms, rarely between the second and third, but readily between the first and fourth or first and fifth carbon atoms, which have approached so near to each other that an oxygen atom is capable of bringing about a closed ring (see Alkylene oxide, p. 367, and Alkylene imines, p. 386, as well as the *strain theory* of *v. Baeyer* in the introduction to the carbocyclic derivatives, Vol. II).

For the arrangement of the atoms in long carbon chains, see p. 33.

It must not be concluded that the preferential formation of rings containing 5 and 6 atoms precludes the formation of rings containing a larger number. Rings containing a large number of atoms occur in nature, *e.g. civetone*, the odoriferous principle of the civet-cat, contains a ring of 17 carbon atoms, and *muscone* one of 16 (Helv. Chim. Acta, **9**, 230, 249). Heterocyclic large ring systems also occur. The vegetable musks (in musk oil and angelica oil) are lactones with 16 and 17 ring members (Ber. **60**, 902: see pp. 429, 454).

A. SATURATED HYDROXYMONO-CARBOXYLIC ACIDS

α-Hydroxy-acids

(1) **Glycollic acid,** *hydroxyacetic acid* [ethanol acid], $CH_2\cdot OH\cdot$-$COOH$, m.p. 80°, occurs in unripe grapes and in the green leaves of virginia creeper, *Ampelopsis hederacea.*

History.—Glycollic acid was first obtained in 1848 by *Strecker* from aminoacetic acid or *glycocoll*—hence the name—by the action of nitrous acid. In 1856 *Debus* discovered it together with glyoxal and glyoxylic acid among the oxidation products obtained from ethyl alcohol by the action of nitric acid. *Wurtz* in 1857 observed its formation in the oxidation of ethylene glycol, and *Kekulé* in 1858 showed how it could be made by boiling a solution of potassium chloroacetate (Ann. **105**, 286: comp. Ber. **16**, 2414: Ann. **200**, 75: Ber. **26**, R. 606).

It is also produced by the action of potassium hydroxide on glyoxal (p. 398); by the reduction of oxalic acid (p. 535), and from diazoacetic ester (p. 458). Its *nitrile* is formed from hydrocyanic acid and formaldehyde (p. 432), and is converted by hydrochloric acid into glycollic acid. It is also formed with hexamethylene tetramine when formaldehyde is warmed with KNC (C. 1900, I. 402). Glycollic acid also appears in the oxidation of glycerol and dextrose by silver oxide.

Glycollic acid crystallizes from acetone. It is very soluble in water and alcohol. Diglycollide and polyglycollide (p. 420) are produced when it is heated. Nitric acid oxidizes it to oxalic acid. When heated with concentrated sulphuric acid, glycollic acid decomposes into trioxymethylene (metaformaldehyde, p. 236), carbon monoxide and water.

Calcium salt, $(CH_2OHCO_2)_2Ca + 3H_2O$; *ethyl ester*, $CH_2OH{\cdot}CO_2{\text -}C_2H_5$, b.p. 160°.

Trichloroethyl alcohol (p. 145) can be regarded as being the chloride of orthoglycollic acid.

(2) **Lactic acid** (*of fermentation*), *α-hydroxypropionic acid, ethylidene lactic acid*, [2-propanol acid], $CH_3CH(OH)CO_2H$, m.p. 18°, b.p. 120°/12 mm. (Ber. **28**, 2597), is isomeric with β-hydroxypropionic acid, hydracrylic acid, $CH_2OH{\cdot}CH_2CO_2H$, which will be discussed later.

Lactic acid is formed by the lactic acid fermentation of lactose, sucrose, gum and starch. It is, therefore, contained in many substances which have soured—*e.g.* in sour milk, in sauerkraut, the lesser centaury (*Erythroca centaurium*) and in gastric contents in cases of pyloric obstruction.

Methods of Formation.—The acid is artificially prepared by the methods already described: (1) from α-propylene glycol; (2) from pyroracemic acid; (5) from α-chloro- or bromo-propionic acid; (6) from alanine; (9) from acetaldehyde and hydrocyanic acid; (13) by heating *iso*malic acid, $CH_3C(OH)(COOH)_2$ (Ber. **26**, R. 7).

Other methods of formation are: the action of heat on dextrose or sucrose with water and 2–3 parts of barium hydroxide at 160°; prolonged contact of hexoses with dilute sodium hydroxide solution (Ber. **41**, 1009); the interaction of pentoses, such as arabinose and xylose with warm potassium hydroxide solution (Ber. **35**, 669); heating α-dichloroacetone, $CH_3{\cdot}CO{\cdot}CHCl_2$, with water at 200°, and oxidation of acetol (p. 393); the two latter methods depend on the transformation of pyroracemic aldehyde into lactic acid by a *Cannizarro* dismutation.

Lactic Acid Fermentation.—This fermentation is induced in sugar solutions by a particular ferment, the lactic acid bacillus, *Bacillus acidi lacti*, which is present in decaying cheese. It proceeds most rapidly at temperatures ranging from 35° to 45° (C. 1897, II. 338). It is noteworthy that the bacillus is very sensitive to free acid. The fermentation is arrested when sufficient lactic acid is produced, but is again renewed when the acid is neutralized. Therefore, zinc or calcium carbonate (C. 1897, II. 20, 937) is added at the beginning, and the lactic acid thus obtained either as the calcium or zinc salt. Should the fermentation continue for some time, the lactic will pass into butyric fermentation, the insoluble calcium lactate will disappear, and the solution will finally contain calcium butyrate (comp. *n*-Butyric acid, p. 304). On the formation of lactic acid as an intermediate product in the fermentation of dextrose to alcohol and CO_2, see Ber. **37**, 421 : Ann. **349**, 125.

Empirically, the lactic acid fermentation is the simplest fermentation, $C_6H_{12}O_6 \longrightarrow 2C_3H_6O_3$, but the intramolecular changes involved in this breakdown are not yet clear. Possibly a reactive form of methylglyoxal, probably a hydrate takes part,

$$C_6H_{12}O_6 \longrightarrow 2CH_3{\cdot}C(OH)_2{\cdot}CHO \longrightarrow 2CH_3{\cdot}CH(OH){\cdot}COOH$$

though methylglyoxal itself is not affected by the lactic acid bacteria (Z. physiol. Chem. **151**, 232).

This mechanism is supported on the one hand by the enzymatic conversion of glucose into methylglyoxal (Biochem. Z. **55**, 495 : **71**, 144), and in the other by the enzymatic dismutation of methylglyoxal into lactic acid (Biochem. Z. **49**, 502 : **51**, 484). The hexosephosphoric esters also play a part as reactive intermediate products (Z. physiol. Chem. **153**, 71).

History.—*Scheele* (1780) discovered lactic acid in sour milk. In 1847 *Liebig* demonstrated that the *sarcolactic acid* found by *Berzelius* (1808) in the fluids of the muscles was different from the *lactic acid of fermentation*. *Wurtz* (1858) described the formation of fermentation lactic acid from α-propylene glycol and air in the presence of platinum black, and considered it a dibasic acid. *Kolbe* (1859) obtained "*lactyl chloride*" by the action of PCl_5 on calcium lactate. This body is identical with chloropropionyl chloride, and lactic acid is therefore monobasic and must be considered as hydroxypropionic acid. Later (1860) *Wurtz* called it a diatomic, monobasic acid, meaning to indicate thereby that one of the two typical hydrogen atoms is more basic than the other. "But it is much more significant when *Kekulé* declares that it is simultaneously an acid and an alcohol" (Ber. **20**, R. 948). *Strecker* was the first to synthesize the acid from synthetic aminolactic acid or alanine, which had also been prepared by him through the interaction of hydrocyanic acid and aldehyde ammonia.

Fermentation lactic acid is a syrup soluble in water, alcohol and ether, and is optically inactive (C. 1905, II. 1527). Placed in a desiccator over sulphuric acid, it partially decomposes into water and its anhydride. When distilled it yields lactide (p. 420), aldehyde, carbon monoxide and water.

Heated to 130° with dilute sulphuric acid, it decomposes into aldehyde and formic acid. Careful oxidation with permanganate, or catalytic dehydrogenation by palladium in the presence of a hydrogen acceptor such as quinone leads to the formation of pyruvic acid, while chromic acid oxidizes it to acetic acid and carbon dioxide.

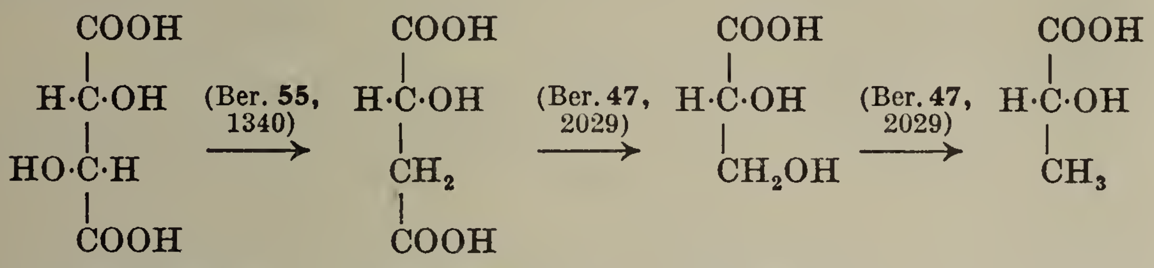
Hydrobromic acid converts it into α-bromopropionic acid, while hydriodic acid reduces lactic acid to propionic acid. With phosphorus pentachloride, α-chloropropionyl chloride is formed.

Salts.—The *sodium salt*, $CH_3{\cdot}CH(OH){\cdot}COONa$, is amorphous, and forms the *disodium* derivative $CH_3{\cdot}CH(ONa){\cdot}COONa$ when heated with sodium. The *calcium salt*, $(C_3H_5O_3)_2Ca$, $5H_2O$, is soluble in ten parts of cold water and more readily in hot. The *zinc salt*, $(C_3H_5O_3)_2Zn$, $3H_2O$, is soluble in 58 parts of cold and 6 of hot water. *Ferrous salt*, $(C_3H_5O_3)_2Fe$, $3H_2O$.

The Optically Active Lactic Acids.—Lactic acid contains an asymmetric carbon atom indicated in the formula $CH_3{\cdot}\overset{*}{C}H(OH)CO_2H$ by the small star. The acid can be resolved by strychnine, morphine, or quinine, into two optically active components,—*dextrorotatory*-lactic acid and *lævorotatory*-lactic acid,—possessing similar but opposite rotary power. The strychnine salt of the lævo-acid crystallizes out first, whilst the quinine salt of the dextro-acid is obtained first (Ber. **24**, R. 794: C. 1906, I. 1150: II. 499).

On mixing solutions of equal quantities of lævo- and dextro-lactate of zinc, the zinc salt of fermentation lactic acid will be produced, and, being more insoluble, will crystallize out. The dextrorotatory modification will remain, if *Penicillium glaucum* is permitted to grow in the solution of inactive ammonium lactate (Ber. **16**, 2720), whilst the lævorotatory modification is produced in the breaking down of a sucrose solution by *Bacillus acidi lævolacti* (Ber. **24**, R. 150).

The optically active lactic acids can be referred to glucose by a series of reactions involving malic and tartaric acids. The prefixes *d-* and *l-* refer to the *stereochemical relationships* of the compounds, and *not to their actual optical activity.* When the configuration of tartaric acid is established, that of lactic acid can be derived therefrom. (Stereochemical series, see Freudenberg, Ber. **47**, 2027: **55**, 1339.) The configuration of *d*-lactic acid is given by the following relations:



d-Tartaric acid (Dextrorotatory). *d*-Malic acid (Dextrorotatory). *d*-Glyceric acid (Lævorotatory). *d*-Lactic acid (Lævorotatory).

Sarcolactic acid, *l*-(+)-*lactic acid, paralactic acid* (*dextrorotatory lactic acid*), was discovered by Berzelius in 1808 in muscle-fluid and shown by Liebig (1848) to be different from the lactic acid of fermentation. It is present in different animal organs, and is most conveniently obtained from Liebig's beef-extract.

Sarcolactic acid is also formed during butyric fermentation (p. 304) by the *granulo-bacillus* and other butyric ferments (C. 1900, I. 777).

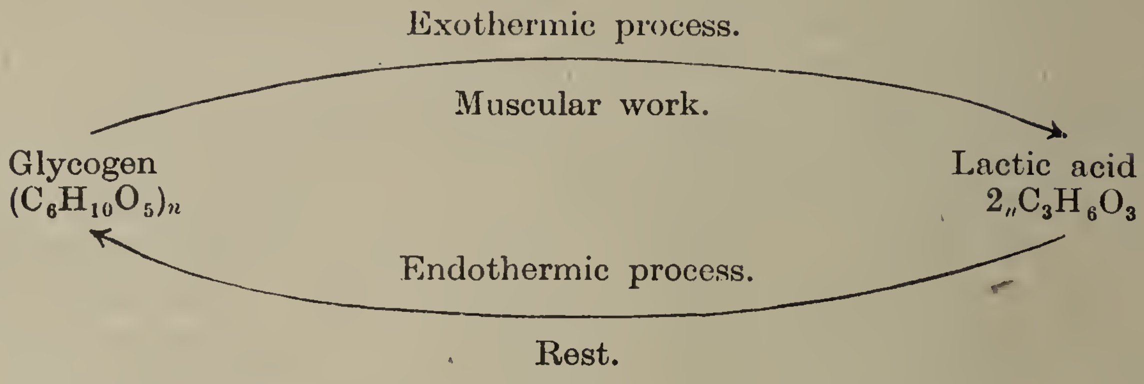
Dextro- and lævo-lactic acid, m.p. 26° approx., are very hygroscopic bodies. Alkali is said to convert the *l*-acid rapidly into the *dl*- modification, whilst the *d*-acid is changed more slowly (Compt. rend. **139**, 203).

The rotation of an approximately 1·24% solution of the crystallized acid in water is $\pm 2{\cdot}24°$ (C. 1906, I. 1150).

The dextro- and lævo-lactates of *zinc* crystallize with 2 molecules of water $(C_3H_5O_3)_2Zn + 2H_2O$. For other salts, see Ber. **29**, R. 899. Zinc *l*-(+)-lactate rotates the plane of polarization to the *left*, whilst the *d*-(−)-lactate rotates it to the *right*: $[\alpha]_D^{20} = \pm 8{\cdot}6°$.

Metabolism.—The importance of lactic acid in metabolism was recognized by Salkowski in 1890. Meyerhof (Ber. 58, 991) has shown that in muscular work the greater part of the energy required is obtained by the exothermic breakdown (+ 27·8 cal.) of glycogen (p. 733) into an equivalent amount of lactic acid. During rest, the lactic acid is again synthesized into carbohydrate and stored as glycogen. The energy required to bring about this endothermic reaction is obtained by the combustion of a part of the lactic acid or of glucose

(*Respiration*). The following scheme shows the part played by lactic acid in metabolism :



Simultaneously with the second process,

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O \text{ (Respiration).}$$

(Neuberg, Z. angew. Chem. **38**, 761 : *Milchsäure und ihre bedeutung für Chemie und Physiologie.*)

Homologous α-Hydroxy-acids.—The homologous α-hydroxy-acids are necessarily, either secondary or tertiary alcohol acids. Glycollic acid is the only primary α-alcohol acid.

(*a*) The *secondary alcohol acids* are generally formed (1) from the corresponding α-halogen fatty acids (method 5) ; (2) from aldehydes and hydrocyanic acid, and subsequent saponification of the nitriles of the hydroxy-acids by means of hydrochloric acid (method 9).

(*b*) The *tertiary hydroxy-acids* result—

(1) From the oxidation of dialkylacetic acids (method 3).

(2) Upon treating α-ketone alcohols with alkalis and air (method 8, p. 411).

(3) By the action of hydrocyanic acid and hydrochloric acid on ketones (method 9).

(4) When zinc and alkyl iodides react with oxalic ester (method 11, p. 411).

(5) From α-ketone-acid esters and magnesium alkyl halides (C. 1902, II. 1359).

Hydroxybutyric acids.—All of the five possible isomers are known ; two of these are α-hydroxy-acids : (1) *α-hydroxybutyric acid*, $CH_3CH_2CH(OH)CO_2H$, m.p. 43°, has been resolved by brucine into its optically active components (Ber. **28**, R. 278, 325, 725).

(2) *α-Hydroxy*iso*butyric acid*, $(CH_3)_2C(OH)COOH$, m.p. 79°, b.p. 212°, is obtained from *iso*butyric acid, from acetone and from oxalic ester (see above). It is produced when *β-iso*amylene glycol is oxidized by nitric acid, and is obtained from α-bromo- and α-amino*iso*butyric acid as well as from amyl pyroracemate and CH_3MgI, and from acetone chloroform.

Trichloro-*tert.*-butyl alcohol, *Acetone chloroform, chloretone* $(CH_3)_2C(OH)$-CCl_3, m.p. 91°, b.p. 167°, is obtained by the union of acetone and chloroform in the presence of alkali hydroxides. It is the chloride of *ortho*-α-hydroxy*iso*butyric acid (p. 280) which stands in the same relation to α-hydroxy*iso*butyric acid that chloroform does to formic acid. Aqueous alkalis convert it into α-hydroxy*iso*butyric acid (*Willgerodt*, Ber. **20**, 2445 : **29**, R. 908 : C. 1898, II. 277 : 1902, I. 176). It acts as an anæsthetic and an antiseptic.

In the presence of phenols and sodium hydroxide solution, acetone and chloroform yield α-phenoxy*iso*butyric acids, $C_6H_5OC(CH_3)_2COOH$ (C. 1906, II. 326).

α-Hydroxyvaleric acids : *α-Hydroxy-*n*-valeric acid*, $CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH$-$(OH){\cdot}CO_2H$, m.p. 28–29° (Ber. **18**, R. 79).

*α-Hydroxy*isovaleric *acid*, $(CH_3)_2{\cdot}CH{\cdot}CH(OH){\cdot}CO_2H$, m.p. 86°, is prepared from dimethyl pyroracemic acid (p. 464) (Ann. **205**, 28 : Ber. **28**, 296 : C. 1902, I. 251).

Methylethylglycollic acid, α-hydroxy-α-methylbutyric acid, $C_2H_5{\cdot}CMe(OH){\cdot}CO_2H$, m.p. 68° (Ann. **204**, 18).

α-Hydroxycaproic acids, *α-hydroxy-*n*-caproic acid*, $CH_3[CH_2]_3CH(OH)$-$COOH$, m.p. 61°, is prepared from α-bromo- or α-amino-*n*-caproic acid.

*α-Hydroxy-*iso*-caproic acid, leucic acid*, $(CH_3)_2CH{\cdot}CH_2CH(OH)COOH$, m.p. 73°, is obtained from leucine (p. 444) by means of nitrous acid (*Strecker*, 1848).

α-Hydroxy-diethylacetic acid, diethyl oxalic acid, $(C_2H_5)_2C(OH){\cdot}COOH$, m.p. 80° (Ann. **200**, 21).

α-*Hydroxy-methyl*iso*propylacetic acid*, $(CH_3)_2CH{\cdot}C(CH_3)(OH)COOH$, m.p. 63° (C. 1898, I. 202).

α-*Hydroxy*-tert.-*butylacetic acid*, $(CH_3)_2C{\cdot}CH(OH)COOH$, m.p. 87°, is obtained from trimethyl pyroracemic acid (p. 464) by reduction.

Higher α-Hydroxy-fatty acids : *β-Diethyllactic acid*, $(C_2H_5)_2CH{\cdot}CH(OH){-}COOH$, m.p. 82°, is prepared from γ-bromo-γ-acetoxy-α-diethyl acetoacetic ester, $(C_2H_5)_2C(COOEt)CO{\cdot}CHBr(OCOCH_3)$, by means of dilute sulphuric acid (Ber. **31**, 2953).

α-*Hydroxy*-n-*caprylic acid*, $CH_3[CH_2]_5CH(OH)COOH$, m.p. 69·5°, is obtained from œnanthol. *Di*-n-*propylglycollic acid*, α-*hydroxy-di*-n-*propylacetic acid*, $(C_3H_7)_2C(OH)COOH$, m.p. 72°, is prepared from butyroin (p. 394) (Ber. **23**, 1273). α-*Hydroxy-di*-iso*propylacetic acid*, $(C_3H_7)C(OH)COOH$, m.p. 111° (Ber. **28**, 2463).

Di-iso*butylglycollic acid* $(C_4H_9)_2C(OH)COOH$, m.p. 114°.

Methylnonylglycollic acid, $(C_9H_{19})C(CH_3)(OH)COOH$, m.p. 46°, is obtained from methyl nonyl ketone (C. 1902, I. 744).

α-Bromo-fatty acids have yielded the following: α-*hydroxylauric acid*, $C_{11}H_{22}(OH)COOH$, m.p. 74° (C. 1904, I. 261) ; α-*hydroxymyristic acid*, $C_{13}H_{26}{-}(OH){\cdot}CO_2H$, m.p. 51° (Ber. **22**, 1747) ; α-*hydroxypalmitic acid*, $C_{15}H_{30}(OH)CO_2H$, m.p. 82° (Ber. **24**, 939) ; α-*hydroxystearic acid*, $C_{17}H_{34}(OH)CO_2H$, m.p. 85° (Ber. **24**, 2388).

In the following pages those α-hydroxy-acid derivatives will be described which belong to glycollic and lactic acids.

Alkyl Derivatives of the α-Hydroxy-acids

An α-hydroxy-acid yields three kinds of alkyl derivatives : *ethers*, *esters* and *ether-esters* :

$CH_2OH{\cdot}COOH$	$CH_2(OC_2H_5){\cdot}COOH$	$CH_2OH{\cdot}COOC_2H_5$	$CH_2(OC_2H_5){\cdot}COOC_2H_5$
Glycollic acid.	Ethoxyacetic acid.	Ethyl glycollate.	Ethyl ethoxyacetate.

(1) The *alkyl-ethers* of the α-hydroxy-acids are obtained (1) by the action of sodium alcoholates on salts of the α-halogen substitution products of the fatty acids ; (2) by the saponification of the ether esters or alkyl ether nitriles (p. 432) of the α-hydroxy-acids.

Methoxyacetic acid, $CH_3OCH_2{\cdot}COOH$, b.p. 198°. **Ethoxyacetic acid**, b.p. 206–207° ; *chloride*, b.p. 128° (J. pr. Chem. [2] 65, 479 : C. 1907, I. 871).

α-Ethoxypropionic acid, $CH_3CH(OC_2H_5){\cdot}CO_2H$, b.p. with partial decomposition 195–198°. It is split up by means of cinchonidine or morphine into its two optical components, which are remarkable for their large rotations.

(2) *Alkyl esters* of the α-hydroxy-acids result (1) on heating the free acids with absolute alcohol ; (2) when the cyclic double esters, the lactides, are heated with alcohols.

Glycollic Acid.—*Methyl ester*, $CH_2(OH)COOCH_3$, b.p. 151°. *Ethyl ester*, b.p. 160°.

Lactic Acid.—*Methyl ester*, $CH_3CH(OH)CO_2CH_3$, b.p. 145°. *Ethyl ester*, b.p. 154·5°.

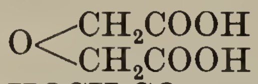
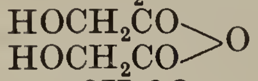
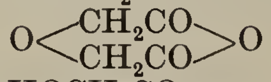
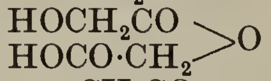
(3) The *ether esters* of the α-hydroxy-acids are produced (1) when sodium alcoholates act on the esters of α-halogen fatty acids ; (2) by the interaction of alkyl halides and the sodium derivatives of the alkyl esters of the α-hydroxy-acids.

Methoxyacetic Acid.—*Methyl ester*, $CH_2(OCH_3){\cdot}COOCH_3$, b.p. 127° ; *ethyl ester*, b.p. 131°. **Ethoxyacetic Acid.**—*Methyl ester*, $CH_2(O{\cdot}C_2H_5)CO{\cdot}OCH_3$, b.p. 148°. *Ethyl ester*, b.p. 152° (Ber. **17**, 486).

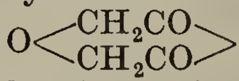
α-Methoxypropionic Acid.—*Methyl ester*, $CH_3CH(OCH_3)COOCH_3$, b.p. 135–138° ; *ethyl ester*, b.p. 135·5°. **Ethoxypropionic Acid.**—*Ethyl ester*, $CH_3{\cdot}CH(OC_2H_5){\cdot}COOC_2H_5$, b.p. 155° (Ann. **197**, 21 : Ber. **40**, 212).

Anhydride Formation of the α-Hydroxy-acids

Since the α-alcohol-acids possess the characteristics of both carboxylic acids and alcohols, they are capable of forming various types of anhydrides. The types of derivative theoretically obtainable may be illustrated by the derivatives of glycollic acid.

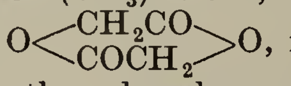
1.	 $O<\begin{matrix}CH_2COOH\\CH_2COOH\end{matrix}$	Alcohol anhydride of glycollic acid: *Diglycollic acid.*
2.	 $\begin{matrix}HOCH_2CO\\HOCH_2CO\end{matrix}>O$	Glycollic anhydride (not known.)
3.	 $O<\begin{matrix}CH_2CO\\CH_2CO\end{matrix}>O$	Alcohol- and acid-anhydride of glycollic acid: *Diglycollic anhydride.*
4.	 $\begin{matrix}HOCH_2CO\\HOCO\cdot CH_2\end{matrix}>O$	Open ester acid: *Glycolloglycollic acid.*
5.	 $O<\begin{matrix}CH_2CO\\COCH_2\end{matrix}>O$	Closed, cyclic double ester of glycollic acid: *Glycollide,* the simplest *Lactide.*

Diglycollic acid, the *alcohol anhydride of glycollic acid,* $C_4H_6O_5$, is formed together with glycollic acid on boiling monochloroacetic acid with lime, baryta, magnesia, or lead oxide, and in the oxidation of diethylene glycol, $O(CH_2\cdot CH_2\cdot OH)_2$ (p. 363). Diglycollic acid crystallizes with H_2O in large rhombic prisms.



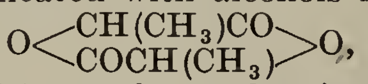
Diglycollic anhydride, $O<\begin{matrix}CH_2CO\\CH_2CO\end{matrix}>O$, m.p. 97°, b.p. 240°, is isomeric with glycollide. It results upon heating diglycollic acid, or by boiling it with acetyl chloride (Ann. **273,** 64).

Glycolloglycollic acid, $CH_2(OH)COOCH_2COOH$, generally termed "*glycollic anhydride,* and **lactyllactic acid,** $CH_3CH(OH)COOCH(CH_3)COOH$, commonly called "*lactic anhydride,*" have not been well studied. They are produced when the free α-hydroxy-acids are heated to 100°, and constitute intermediate steps in the lactide formation (Ber. **23,** R. 325). Distillation of lactic acid produces lactyl lactic acid, lactide, and also *lactyl lactic lactic acid,* $CH_3CH(OH\text{-}.COOCH(CH_3)COOCH(CH_3)COOH$, m.p. 39°, b.p. 235–240° (C. 1905, I. 862).



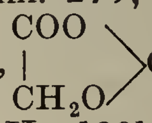
Diglycollide, $O<\begin{matrix}CH_2CO\\COCH_2\end{matrix}>O$, m.p. 86°, is produced when polyglycollide is distilled under greatly reduced pressure. When heated at the ordinary pressure, or if kept, it reverts to polyglycollide, from which it differs by its lower melting point and ready solubility in chloroform. It combines readily with water (Ann. **279,** 45).

Polyglycollide, $(C_2H_2O_2)_x$, m.p. 223°, is formed on heating glycollic acid, and when dry sodium chloroacetate is heated alone to 150°. It passes into glycollic esters when heated with alcohols in sealed tubes (Ann. **279,** 45).

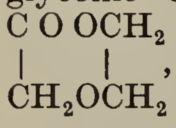


Lactide, $O<\begin{matrix}CH(CH_3)CO\\COCH(CH_3)\end{matrix}>O$, m.p. 125°, b.p. 255°, b.p. 138°/12 mm., (Ber. **28,** 2595), results on heating lactic acid under diminished pressure. It can be recrystallized from chloroform (Ann. **167,** 318: Ber. **25,** 3511: **28,** 2595). d- and l-*Lactide,* m.p. 95° (C. 1906, I. 1329). The optical rotation of the lactic acids is increased greatly by lactide formation.

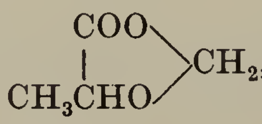
Homologous lactides, see Ber. **26,** 263; Ann. **279,** 100.



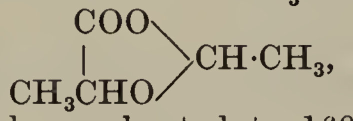
Cyclic Ether Esters.—*Methylene glycollate,* $\begin{matrix}COO\\|\\CH_2O\end{matrix}>CH_2$, is obtained from glycollic acid and formaldehyde (C. 1901, II. 1261). *Ethylene glycollate,*



$\begin{matrix}C\,O\,OCH_2\\|\qquad|\\CH_2OCH_2\end{matrix}$, m.p. 31°, b.p. 214° (Ber. **27,** 2945).



Methylene lactate, $\begin{matrix}COO\\|\\CH_3CHO\end{matrix}>CH_2$, b.p. 153° (Ber. **28,** R. 180). *Ethylidene*



lactate, $\begin{matrix}COO\\|\\CH_3CHO\end{matrix}>CH\cdot CH_3$, b.p. 151°, is produced when lactic acid and acetaldehyde are heated to 160°. Its hexachloro-derivative is chloralide (below).

Acid Esters of the α-Hydroxy-acids

Nitroglycollic acid, m.p. 54°, results, together with nitroglycollyl glycollic acid, $NO_2OCH_2COOCH_2COOH$, from glycollic acid and nitrosulphuric acid.

Nitrolactic acid, $CH_3CH(ONO_2)COOH$, is a yellow liquid, decomposing at the ordinary temperature into oxalic and hydrocyanic acids (Ber. **12**, 1837 : C. 1903, II. 488 : 1904, I. 434). Monohalogen acetic acid (p. 334) and α-halogen propionic acid (p. 335) are looked on as being haloid acid esters of α-hydroxy-acids.

Acetoxyacetic Acid.—*Acetylglycollic acid,* $CH_2O(COCH_3)COOH$, m.p. 67°, b.p. 145°/12 mm., is obtained from glycollic acid and acetic anhydrides ; *chloride,* b.p. 54°/14 mm. ; *ethyl ester,* $CH_2O(COCH_3)COOC_2H_5$, b.p. 179°.

α-Acetoxypropionic Acid.—*Acetyllactic acid,* $CH_3CH(OCOCH_3)COOH$, m.p. 57–60°, b.p. 127°/11 mm., is prepared from lactic acid and acetyl chloride ; *chloride,* b.p. 56°/11 mm. (Ber. **36**, 466 : **37**, 3971 : **38**, 719 : C. 1905, I. 1373).

Halogen α-Hydroxy-acids

β-Monohalogen Lactic Acids.—*β-Chlorolactic acid,* $CH_2ClCH(OH)CO_2H$, m.p. 78°. *β-Bromolactic acid,* $CH_2BrCHOHCO_2H$, m.p. 89°. *β-Iodolactic acid,* $CH_2ICH(OH)CO_2H$, m.p. 100°. These three acids are prepared by adding hydrogen chloride, bromide or iodide to glycidic acid, $\overline{\mathrm{CH_2CH(O}}\mathrm{)CO_2H}$.

β-Chlorolactic acid is also formed from monochloroacetaldehyde by the action of hydrocyanic acid and by the oxidation of epichlorohydrin, $\overline{\mathrm{CH_2CH(O}}\mathrm{)CH_2Cl}$, and α-chlorohydrin, $CH_2ClCH(OH)\cdot CH_2OH$, with concentrated HNO_3 ; as well as by the addition of hypochlorous acid to acrylic acid (together with α-chlorohydracrylic acid).

Silver oxide converts it into glyceric acid ; when reduced with hydriodic acid it yields β-iodopropionic acid. Heated with alcoholic potassium hydroxide it is again changed to glycidic acid, just as ethylene oxide is obtained from glycol chlorohydrin (p. 367).

Higher halogen substitution products of the α-hydroxy-acids have been prepared by the treatment of halogen aldehydes, such as dichloroacetaldehyde, chloral, bromal, and trichlorobutyric aldehyde, with hydrocyanic acid and hydrochloric acid. Trichlorolactic acid has been the most thoroughly studied.

β-Dichlorolactic acid, $CHCl_2\cdot CH(OH)\cdot CO_2H$, m.p. 77°.

β-Trichlorolactic acid, $CCl_3\cdot CH(OH)CO_2H$, m.p. 105–110°, is soluble in water, alcohol and ether. Alkalis easily change it into chloral, chloroform and formic acid. Zinc and hydrochloric acid reduce it to dichloro- and mono-chloroacrylic acids (p. 342).

Because trichlorolactic acid yields chloral without difficulty, it is converted quite readily, by different reactions, into derivatives of chloral, and also of glyoxal, probably by decomposition into dichloroaldehyde and CO_2, *e.g.* it forms glyoxime with hydroxylamine, and glycosine with ammonia (p. 399, and Ber. **17**, 1997).

Ethyl trichlorolactate, $CCl_3CH(OH)COOC_2H_5$, m.p. 66°, b.p. 235°, is prepared from chloral cyanohydrin with alcohol and sulphuric or hydrochloric acid (Ber. **18**, 754).

Chloralide, trichloroethylidene trichlorolactate, $CCl_3\cdot CH\!<\!\substack{O\\CO_2}\!>\!CH\cdot CCl_3$, m.p. 114°, b.p. 272°, was first prepared by heating chloral with fuming sulphuric acid to 105°, and subsequently when trichlorolactic acid was heated to 150° with chloral. When heated to 140° with alcohol, it breaks up into trichlorolactic ester and chloral alcoholate (*Wallach,* Ann. **193**, 1). Chloral also unites with lactic and other hydroxy-acids, glycollic, malic, salicylic, etc., forming compounds very similar to that with trichlorolactic acid, known as *chloralides* (Ann. **193**, 1).

Tribromolactic acid, $CBr_3\cdot CH(OH)CO_2H$, m.p. 141–143°, unites with chloral and bromal to corresponding chloralides and bromalides.

Trichlorovalerolactic acid, $CH_3CCl_2CHCl\cdot CH(OH)\cdot CO_2H$, m.p. 140° (Ann. **179**, 99).

β-Hydroxycarboxylic Acids

Generally the β-hydroxycarboxylic acids, when heated, part with water and become converted into unsaturated olefine carboxylic acids :

$$\underset{\text{Hydracrylic acid.}}{CH_2OH\cdot CH_2\cdot CO_2H} \xrightarrow{-H_2O} \underset{\text{Acrylic acid.}}{CH_2{=}CHCO_2H.}$$

In the case of the higher homologues of ethylene lactic acid, when water is eliminated, both αβ- and βγ-olefine carboxylic acids (Ber. **26**, 2079) result.

Only under very special conditions (agitation of the sodium salts of β-halogen-fatty acids in chloroform) is it possible to obtain the internal anhydrides (*β-lactones*) of the β-hydroxy-acids (see p. 333). They are more readily obtained by the addition of ketens to carbonyl compounds.

$$CH_2Cl{\cdot}CH_2{\cdot}COOH \longrightarrow \overset{\ulcorner\!-\!-O-\!-\!\urcorner}{CH_2{\cdot}CH_2{\cdot}CO}$$

α-Dialkyl-β-hydroxy-acids and their esters are prepared from the dialkylacetoacetic esters by reduction, and from aldehydes, and α-bromodialkylacetic esters by the action of zinc. Those which possess no hydrogen atom in the α-position free to take part in the splitting off of water decompose in various ways: when heated, some are converted into a mixture of aldehydes and dialkylacetic acids; others yield semilactides, like the α-hydroxy-acids (p. 420) (C. 1904, I. 1134):

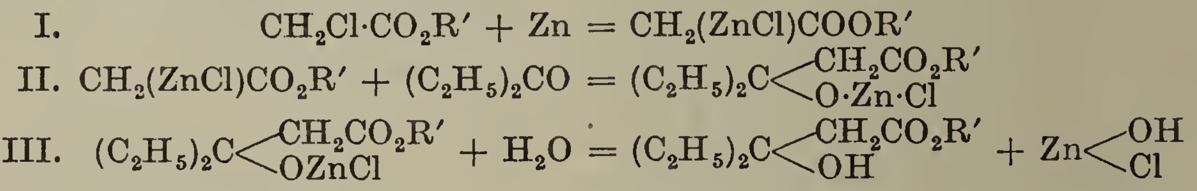
$$\underset{\text{β-Hydroxy-α-diethylbutyric acid.}}{CH_3CH(OH)C(C_2H_5)_2COOH} = CH_3CHO + \underset{\text{Diethylacetic acid.}}{CH(C_2H_5)_2COOH}$$

$$\underset{\text{Hydroxypivalic acid.}}{CH_2(OH)C(CH_3)_2COOH}$$

$$\longrightarrow CH_2(OH)C(CH_3)_2COO[CH_2C(CH_3)_2COO]_4CH_2{\cdot}C(CH_3)_2COOH$$

The esters of such acids containing free hydrogen atoms attached to a carbon atom in the γ-position react with P_2O_5 in a benzene solution and form βγ-olefine carboxylic acids; in other cases atomic migration occurs, and αβ-olefine carboxylic acids result (p. 338) (C. 1906, I. 999: II. 318).

β-Hydroxy-acids are produced (1) in the oxidation of primary-secondary and primary-tertiary glycols; (2) (p. 466) by the reduction of β-ketonecarboxylic esters (secondary hydroxy-acids); and (3) on boiling βγ-olefine carboxylic acids with sodium hydroxide. (4) Zinc and the esters of the monohalogen fatty acids—*e.g.* bromo*iso*butyric ester—combine with aldehydes (*iso*butyraldehyde) to form secondary β-hydroxy-acids, and with ketones to form tertiary β-hydroxy-acids (Ber. **28**, 2838, 2842: C. 1906, I. 999: II. 318). In these reactions the following stages can be recognized:



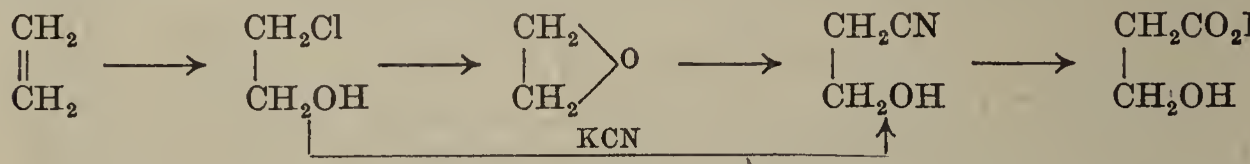
$$\text{I.}\quad CH_2Cl{\cdot}CO_2R' + Zn = CH_2(ZnCl)COOR'$$

$$\text{II.}\quad CH_2(ZnCl)CO_2R' + (C_2H_5)_2CO = (C_2H_5)_2C\!<\!\begin{smallmatrix}CH_2CO_2R'\\ O{\cdot}Zn{\cdot}Cl\end{smallmatrix}$$

$$\text{III.}\quad (C_2H_5)_2C\!<\!\begin{smallmatrix}CH_2CO_2R'\\ OZnCl\end{smallmatrix} + H_2O = (C_2H_5)_2C\!<\!\begin{smallmatrix}CH_2CO_2R'\\ OH\end{smallmatrix} + Zn\!<\!\begin{smallmatrix}OH\\ Cl\end{smallmatrix}$$

This reaction resembles in all its stages the preparation of tertiary alcohols from ketones and alkyl magnesium halides (p. 133).

Hydracrylic acid, *ethylene lactic acid,* [3-propanol acid], $CH_2(OH){\cdot}CH_2{\cdot}CO_2H$, is isomeric with ordinary lactic acid, and is obtained (1) by the oxidation of trimethylene glycol; (2) from β-iodopropionic acid, or β-chloropropionic acid, with moist silver oxide; (3) from acrylic acid by heating with aqueous sodium hydroxide to 100°; (4) by the saponification of ethylene cyanohydrin with hydrochloric acid. This reaction enables the synthesis of hydracrylic acid from ethylene:



The free acid forms a non-crystallizable, thick syrup. When heated alone, or when boiled with sulphuric acid (diluted with 1 part H_2O), it loses water and forms acrylic acid (hence the name hydracrylic acid).

Hydriodic acid converts it into β-iodopropionic acid. It yields oxalic acid and carbon dioxide when oxidized with chromic acid or nitric acid.

The *sodium salt*, $CH_2(OH)CH_2CO_2Na$, m.p. 142–143°, and the *calcium salt* $(C_3H_5O_3)_2Ca + 2H_2O$, m.p. (anhydrous) 140–150°, when heated above their melting points pass into the corresponding acrylates. The *zinc salt*, $(C_3H_5O_3)_2$-$Zn + 4H_2O$, is soluble in water and alcohol, whereas the latter precipitates zinc salts of the isomeric acids.

β-Amyloxypropionic acid, $C_5H_{11}OCH_2CH_2COOH$, b.p. 140°/20 mm., yields the diamyl-ether of tetramethylene glycol, when its sodium salt is electrolysed (p. 364) (C. 1905, I. 1698).

β-Hydroxybutyric acid, [3-butanol acid], $CH_3CH(OH)\overset{*}{C}H_2CO_2H$, is formed (1) by the oxidation of aldol (p. 390); (2) by the reduction of acetoacetic ester (p. 473) with sodium amalgam; (3) from α-propylene chlorohydrin, $CH_3CH(OH)$-CH_2Cl, by the action of KCN and subsequent hydrolysis of the cyanide. It is a syrup and is volatile in steam. Heat decomposes it into water and crotonic acid, $CH_3{\cdot}CH:CHCOOH$. Conversely, crotonic ester unites with alcohol in the presence of C_2H_5ONa to form β-ethyoxybutyric ester, $C_2H_5O{\cdot}CH(CH_3)CH_2$-$CO_2R$ (Ber. **33**, 3329). The racemic acid is split by means of its quinine salts; the *lævo*-rotatory component $[\alpha]_D = -24{\cdot}9°$ separates out, and the *dextro*-rotatory component is obtained from the mother liquor. An optically active β-hydroxybutyric acid has been isolated from diabetic urine (Ber. **18**, R. 451).

β-Hydroxy*iso*butyric acid, *α-methylhydracrylic acid*, $CH_2OH{\cdot}CHMe{\cdot}COOH$, is obtained from α-bromopropionic ester, trioxymethylene and zinc. *Ethyl ester*, b.p. 79°/7 mm. (Ann. Chim. [8] **17**, 390.)

Hydroxyvaleric Acids.—*β-Hydroxy-*n*-valeric acid*, $CH_3CH_2CH(OH){\cdot}CH_2$-$CO_2H$ (Ann. **283**, 74, 94). *β-Hydroxy-α-methylbutyric acid*, $CH_3CH(OH)CH(CH_3)$-CO_2H (Ann. **250**, 244). *α-Ethylhydracrylic acid* is a syrup: *ethyl ester*, b.p. 96°/3 mm., is obtained from trioxymethylene and α-bromobutyric acid in benzene solution with zinc (C. 1905, II. 45, 540). *β-Hydroxy*isovaleric* acid*, $(CH_3)_2C(OH)$-$CH_2{\cdot}CO_2H$, results when *iso*valeric acid is oxidized with $KMnO_4$ (Ann. **200**, 273). *α-Dimethylhydracrylic acid, hydroxypivalic acid*, $HO{\cdot}CH_2C(CH_3)_2COOH$, m.p. 124°; *ethyl ester*, b.p. 86°/16 mm., is obtained from trioxymethylene, bromo*iso*butyric ester and zinc (C. 1902, I. 643). *Acetoxypivalic chloride* (C. 1908, I. 1531).

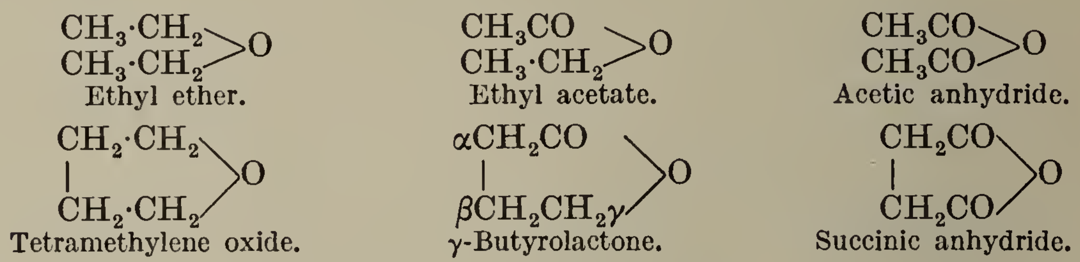
Hydroxycaproic Acids.—*β-Hydroxy-*n*-caproic acid*, $CH_3CH_2CH_2CH(OH)$-CH_2CO_2H, is formed on boiling hydrosorbic acid with sodium hydroxide (Ann. **283**, 124). *β-Hydroxy-α-ethylbutyric acid*, $CH_3CH(OH)CH(C_2H_5)CO_2H$ (Ann. **188**, 240). *β-Hydroxy-α-methylvaleric acid*, $CH_3CH_2CH(OH)CH(CH_3)CO_2H$ (Ber. **20**, 1321). *β-Hydroxy*isocaproic* acid*, $(CH_3)_2CHCH(OH)CH_2CO_2H$ (Ber. **29**, R. 667). *ββ-Methylethylhydracrylic acid* is obtained by oxidation of methyl ethyl allyl carbinol (C. 1900, I. 1069), *α-Methyl-β-ethylhydracrylic acid* is a syrup. *α-Methyl-α-ethylhydracrylic acid*, m.p. 56°. *α-Propylhydracrylic acid* is a syrup. *α-*iso*Propylhydracrylic acid*, m.p. 64°. *ααβ-Trimethylhydracrylic acid*, m.p. 31°, b.p. 148°/5 mm., is obtained as an ester (method of formation, No. 12, p. 411).

Hydroxyheptoic Acids.—*β-Hydroxy*iso*heptoic acid*, $(CH_3)_2CHCH_2CH(OH)$-CH_2CO_2H, m.p. 64° (Ann. **283**, 143). *β-Methylpropylhydracrylic acid*, (CH_3)-$(C_3H_7)C(OH)CH_2CO_2H$, is produced in the oxidation of methyl allyl propyl carbinol (J. pr. Chem. [2] **23**, 267). *β-Diethylhydracrylic acid*, $(C_2H_5)_2C(OH)$-CH_2CO_2H, results from the oxidation of diethyl allyl carbinol, (J. pr. Chem. [2] **23**, 201) (p. 152). *α-Methylethyl-β-hydroxybutyric acid*, $CH_3CH(OH)C(CH_3)$-$(C_2H_5)CO_2H$ (Ann. **188**, 266). *Tetramethylhydracrylic acid*, $(CH_3)_2C(OH)C(CH_3)_2$-CO_2H, m.p. 152°, is prepared from acetone, bromo*iso*butyric ester and zinc. It yields CO_2 and dimethyl*iso*propylcarbinol when heated. The ester and P_2O_5 yield dimethyl*iso*propenylacetic acid (Ber. **28**, 2829: C. 1906, I. 909). *α-Dimethyl-β-ethylhydracrylic acid*, $C_2H_5CH(OH)C(CH_3)_2COOH$, m.p. 103° (C. 1901, I. 1196).

*β-Hydroxy*isooctylic* acid*, $(CH_3)_2CHCH_2CH_2CH(OH)CH_2CO_2H$, m.p. 36° (Ann. **283**, 287). *β-Hydroxy-α-methylpropylbutyric acid*, $CH_3CH(OH)C(CH_3)(C_3H_7)CO_2H$ (Ann. **226**, 288). *β-Hydroxy-α-diethylbutyric acid*, $CH_3CH(OH)C(C_2H_5)_2CO_2H$ (Ann. **201**, 65: **266**, 98). *α-Dimethyl-β-*iso*propylhydracrylic acid*, $(CH_3)_2CH{\cdot}CH$-$(OH){\cdot}C(CH_3)_2{\cdot}CO_2H$, m.p. 92° (Ber. **28**, 2843), is obtained also by oxidation of the corresponding glycol or aldol (p. 391) (C. 1902, I. 461).

The γ- and δ-Hydroxy-acids and their Cyclic Esters, the γ- and δ-Lactones

The γ- and δ-hydroxy-acids are distinguished from the α- and β-hydroxy-acids by the fact mentioned (p. 414) that they are readily capable of forming simple cyclic esters, when the carboxyl group enters into reaction with the alcoholic hydroxyl group. This is a reaction that is accelerated by mineral acids as in the case of the formation of the ordinary fatty acid esters. The cyclic esters of the γ- and δ-hydroxy-acids are called *γ-Lactones* and *δ-Lactones.* In the first there is a chain of four, in the second a chain of five carbon atoms closed by oxygen. They sustain the same relation to the oxides of the γ- and δ-glycols, and to the anhydrides of the γ- and δ-dicarboxylic acids, that the open carboxylic esters bear to the ethers of the alcohols and fatty acid anhydrides. The following scheme represents these relations:



Ethyl ether. Ethyl acetate. Acetic anhydride.

Tetramethylene oxide. γ-Butyrolactone. Succinic anhydride.

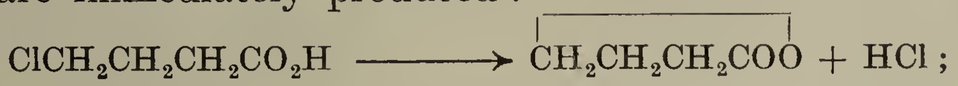
This lactone formation occurs more or less easily, depending upon the constitution of the γ-hydroxy-acids. The same causes which influence the anhydride formation with saturated and unsaturated dicarboxylic acids (*q.v.*), exert their power with the γ-hydroxy-acids. It has been seen " that increasing magnitude or number of hydrocarbon residues in the carbon chains closed by oxygen favours the intramolecular splitting-off of water among the γ-hydroxy-acids " (Ber. **24**, 1237). When the γ-hydroxy-acids are separated from their salts by mineral acids they break down, especially on warming, almost immediately into water and lactones. When the latter are boiled with alkali carbonates they are converted into salts of the hydroxy-acids. This is more readily accomplished through the agency of the alkali hydroxides. The γ-lactones are characterized by great stability, being only partially converted into hydroxy-acids by water, after protracted boiling, whereas those of the δ-variety gradually absorb water at the ordinary temperature and soon react acid (Ber. **16**, 373).

History.—The first (1873) discovered aliphatic lactone was butyrolactone, obtained by *Saytzeff*, who, however, regarded it as the dialdehyde of succinic acid. *Erlenmeyer*, Sr. (1880), expressed the opinion that lactones could only exist when they contained the group $\overline{\mathrm{C{-}C{-}C{-}COO}}$, which is present in the anhydride of succinic acid (Ber. **13**, 305). Almost immediately afterwards *J. Bredt* demonstrated that *iso*caprolactone, from pyroterebic acid, was in fact a γ-lactone (Ber. **13**, 748). *Fittig*, as the result of a series of excellent investigations, established the genetic relations of the lactones to the hydroxy-acids and unsaturated acids, and taught how this class of bodies could be produced by new methods. *E. Fischer* has shown that polyhydroxylactones play an especially important rôle in the synthesis of the various varieties of sugar, *General methods of formation of the γ-hydroxycarboxylic acids and the γ-lactones :*

(1) By the reduction of the γ-ketone carboxylic acids with sodium amalgam :

$$\underset{\text{Lævulinic acid.}}{CH_3CO{\cdot}CH_2CH_2COOH} + 2H = \underset{\gamma\text{-Hydroxyvaleric acid.}}{CH_3CH(OH){\cdot}CH_2CH_2CO_2H.}$$

(2) From the γ-halogen fatty acids : (*a*) by distillation, when the lactones are immediately produced :



$$ClCH_2CH_2CH_2CO_2H \longrightarrow CH_2CH_2CH_2COO + HCl\,;$$

(*b*) by boiling them with water, or with alkali hydroxides, or carbonates. In the latter case γ-lactones are even produced in the cold.

(3) From unsaturated acids in which the double union occurs in the βγ- or γδ-position, that is, from the Δ^{β}- or Δ^{γ}- unsaturated acids :

(*a*) by distillation ;

(*b*) by digestion with hydrobromic acid, when an addition and separation of hydrogen bromide occur ;

(*c*) by digestion with dilute sulphuric acid (Ber. **16,** 373 : **18,** R. 229 : **29,** 1857) :

$$\overset{\delta}{C}H_2{=}\overset{\gamma}{C}H\overset{\beta}{C}H_2\overset{\alpha}{C}H_2CO_2H \longrightarrow CH_3CHCH_2CH_2COO$$

Allyl acetic acid. γ-Valerolactone.

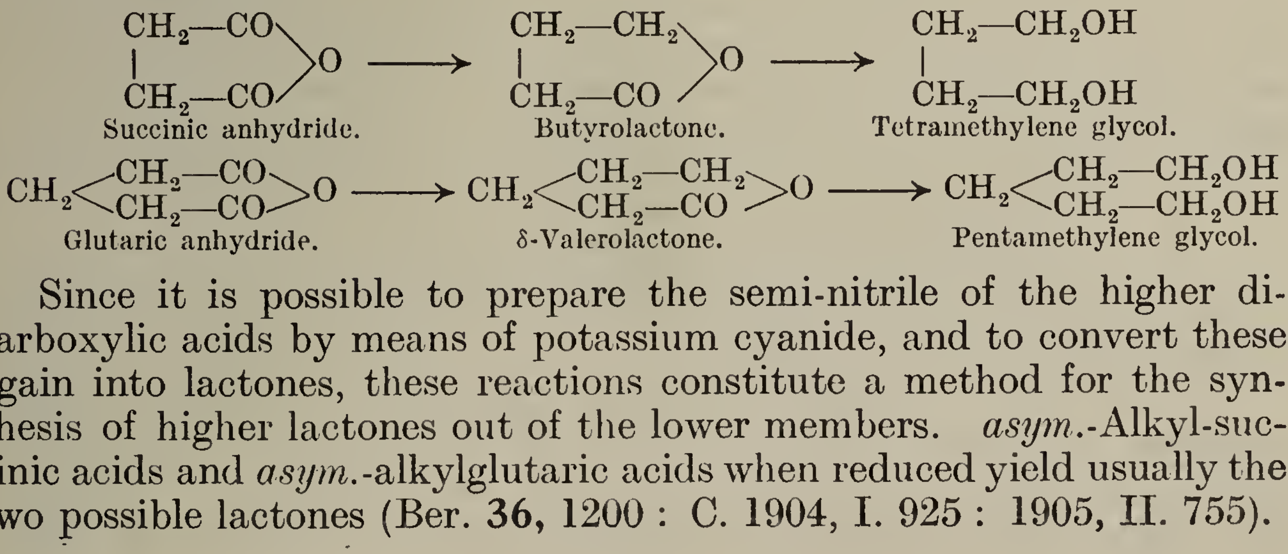
(4) By the decomposition of γ-lactone carboxylic acids into γ-lactones and CO_2, by distillation, whereby the isomeric unsaturated acids are also produced (p. 337) :

$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>C{\cdot}CH(COOH){\cdot}CH_2COO \longrightarrow \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>C{\cdot}CH_2{\cdot}CH_2{\cdot}COO + CO_2.$$

Terebic acid. *iso*Caprolactone.

By similar reactions lactones can be formed by decomposition of the condensation product of glycol halogenhydrin (p. 369), (*a*) with sodium acetoacetic ester, and (*b*) sodium malonic ester.

(5) Reduction of the derivatives of dicarboxylic acids leads to the formation of glycols (Method 6*b*, p. 360). Hydroxy-acids are formed as intermediate products during reduction ; in the cases of esters, chlorides, or anhydrides of the succinic and glutaric acid series, reduction with sodium amalgam or aluminium amalgam, or with sodium and alcohol, gives rise to a 5–50% yield of γ- and δ-hydroxy-acids or their lactones.



Succinic anhydride. Butyrolactone. Tetramethylene glycol.

Glutaric anhydride. δ-Valerolactone. Pentamethylene glycol.

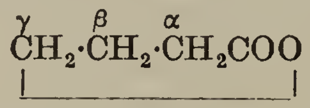
Since it is possible to prepare the semi-nitrile of the higher dicarboxylic acids by means of potassium cyanide, and to convert these again into lactones, these reactions constitute a method for the synthesis of higher lactones out of the lower members. *asym.*-Alkyl-succinic acids and *asym.*-alkylglutaric acids when reduced yield usually the two possible lactones (Ber. **36,** 1200 : C. 1904, I. 925 : 1905, II. 755).

Nucleus-synthetic Methods of Formation:

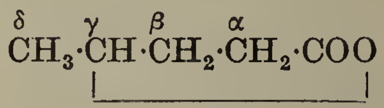
(6) The action of zinc alkyls on the chlorides of dibasic acids, or of magnesium alkyl halides on γ-ketonic esters (C. 1902, II. 1359).

(7) Action of potassium cyanide on γ-halohydrins, and subsequent saponification of the resulting nitriles.

Nomenclature.—γ-Lactones may be viewed as α-, β-, and γ-alkyl substitution products of butyrolactone, and may be named accordingly; thus, γ-methyl butyrolactone for valerolactone:



$$\underbrace{\overset{\gamma}{C}H_2\cdot\overset{\beta}{C}H_2\cdot\overset{\alpha}{C}H_2COO}$$



$$\overset{\delta}{C}H_3\cdot\underbrace{\overset{\gamma}{C}H\cdot\overset{\beta}{C}H_2\cdot\overset{\alpha}{C}H_2\cdot COO}$$

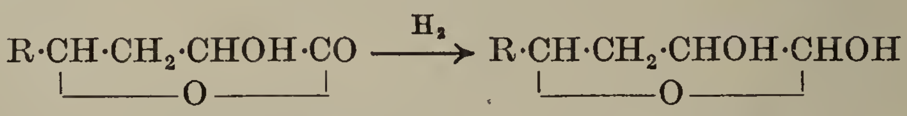
The "Geneva names" terminate in "olide"; thus, butyrolactone = [butanolide]; valerolactone = [1 : 4-pentanolide].

Properties of the γ- and δ-Lactones.—They are usually liquid bodies, easily soluble in water, alcohol, and ether. They possess a neutral reaction, and a faintly aromatic odour, and can be distilled without decomposition. The alkali carbonates precipitate them from their aqueous solution in the form of oils.

Reactions.—(1) They are partially converted into the corresponding hydroxy-acids when boiled with water. A state of equilibrium arises here, the position of which is much influenced by the number of alkyl groups contained in the γ-lactones. (2) The lactones are changed with difficulty by the alkali carbonates into salts of the corresponding hydroxy-acids (Ber. 25, R. 845), whereas the alkali hydroxides and barium hydroxide solution effect this more readily. (3) Many γ-lactones combine with the halogen acids, forming the corresponding γ-halogen fatty acids; others do not do this. In the latter the lactone union is easily severed on allowing hydrochloric or hydrobromic acid to act on the lactones in the presence of alcohol, when the alkyl esters of the corresponding γ-chloro- and γ-bromo-fatty acids are formed (Ber. **16**, 513). Lactones are converted into the esters of hydroxy-acids by heating them with sulphuric acid in alcoholic solution (Ber. **33**, 860).

(4) The γ-lactones unite with ammonia, without separation of water (p. 431). Similarly, hydrazine gives characteristic crystalline addition-products, easily split up into hydrazine and lactone (C. 1905, I. 1221).

5. Sodium and alcohol reduces the lactones to glycols. The γ-lactones of the $\alpha\gamma$-dihydroxy-acids are of theoretical importance as they form simple models of the hexonic lactones, and like them, are reduced by sodium amalgam to, probably, the $\alpha\gamma$-dihydroxyaldehyde (Ber. **54**, 2634):

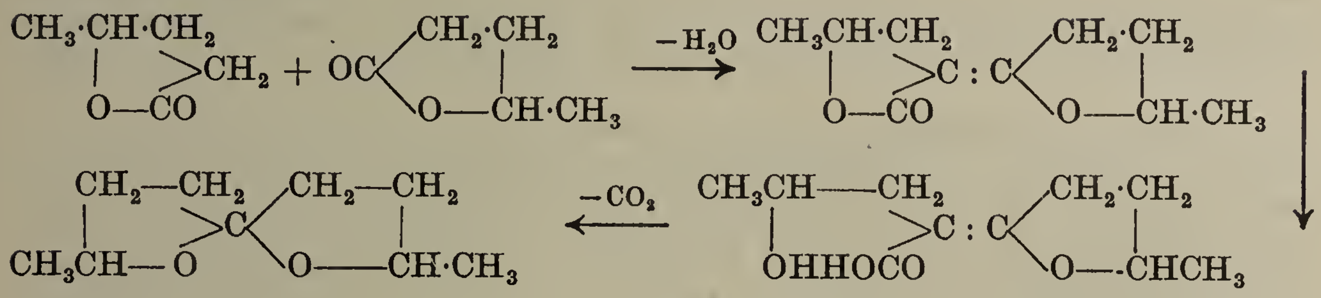


$$R\cdot\underbrace{CH\cdot CH_2\cdot CHOH\cdot CO}_{O} \xrightarrow{H_2} R\cdot\underbrace{CH\cdot CH_2\cdot CHOH\cdot CHOH}_{O}$$

(6) Potassium cyanide unites with the formation of potassium salts of the nitrile-carboxylic acids.

(7) The lactones condense under the influence of sodium and sodium alcoholate to compounds which give up water when treated with acids to form substances composed of two lactone residues. When boiled with bases, these bodies are converted to hydroxycarboxylic acids,

which split off carbon dioxide, forming *oxetones* (*q.v.*), derivatives of dihydroxyketones :



γ-Lactones

Butyrolactone [butanolide], $CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}COO$, b.p. 206°, has been obtained (1) by allowing sodium amalgam and glacial acetic acid to act on succinyl chloride in ethereal solution (Ann. **171**, 261 : Ber. **29**, 1192) ; (2) from *β*-formylpropionic acid (p. 457) by reduction ; (3) from butyrolactonecarboxylic acid (*q.v.*), by the splitting-off of CO_2 (Ber. **16**, 2592) ; (4) by the distillation of *γ*-chlorobutyric acid (Ber. **19**, R. 13) ; (5) from hydroxyethylacetoacetic ester (from ethylene chlorohydrin and acetoacetic ester) by decomposing it with barium hydroxide (Ber. **18**, R. 26) ; (6) by treating *γ*-phenoxybutyric acid with hydrobromic acid (Ber. **29**, R. 286).

Lactones, $C_5H_8O_2$; *γ-Valerolactone, γ-methyl butyrolactone,* [1 : 4-pentanolide], $CH_3{\cdot}CH{\cdot}CH_2{\cdot}CH_2{\cdot}COO$, b.p. 206°, occurs in crude wood vinegar, and may be prepared (1) by the reduction of lævulinic acid, $CH_3CO{\cdot}CH_2CH_2CO_2H$ (Ann. **208**, 104) ; (2) by boiling allylacetic acid with dilute sulphuric acid ; (3) when *γ*-bromovaleric acid is boiled with water ; (4) on heating *γ*-hydroxypropyl malonic lactone to 220° C. (Ann. **216**, 56) ; (5) and in small quantities when methyl paraconic acid is distilled (Ann. **255**, 25). Dilute nitric acid oxidizes *γ*-valerolactone to succinic acid, whilst HI converts it into *n*-valeric acid.

α-Methylbutyrolactone, $CH_2CH_2CH(CH_3)COO$, b.p. 201°, is obtained from pyrotartaric chloride or anhydride by reduction (Ber. **28**, 10 : **29**, 1194 : C. 1905, II. 755).

Lactones : $C_6H_{10}O_2$. *γ-n-Caprolactone, γ-ethylbutyrolactone,* [1 : 4-Hexanolide], $CH_3{\cdot}CH_2CHCH_2CH_2COO$, b.p. 220°, is formed by the general methods 2, 3, and 4. It also appears in the reduction of gluconic acid, metasaccharic acid and galactonic acid by hydriodic acid (Ber. **17**, 1300 : **18**, 642, 1555).

α-Ethylbutyrolactone, b.p. 219°, is prepared from ethyl succinic anhydride and from α-ethyl-α-ethoxyacetoacetic ester.

βγ-Dimethylbutyrolactone, b.p. 209°, is obtained from *β*-acetobutyric acid.

αγ-Dimethylbutyrolactone, b.p. 206°, is obtained from aceto*iso*butyric acid.

αα-Dimethylbutyrolactone, b.p. 202°, is formed, together with its isomer *ββ-dimethylbutyrolactone,* by reduction of *unsym.*-dimethylsuccinic ester as anhydride (C. 1904, I. 925 : II. 587).

iso*Caprolactone, γ-dimethylbutyrolactone,* $(CH_3)_2CCH_2CH_2COO$, m.p. 7°, b.p. 207°, is produced together with pyroterebic acid in the distillation of terebic acid. (See general method 4, p. 425.) Pyroterebic acid itself passes on long boiling into *iso*caprolactone. It can also be obtained from *iso*butyric aldehyde, malonic acid and acetic anhydride (Ber. **29**, R. 667).

Lactones : $C_7H_{12}O_2$ *γ-n-Heptolactone, γ-n-Propylbutyrolactone,* CH_3CH_2-$CH_2CHCH_2CH_2COO$, b.p. 235°, is obtained from *γ*-bromœnanthic acid, from *n*-propylparaconic acid, and from dextrose carboxylic acid, as well as from galactose carboxylic acid on treatment with hydriodic acid (Ber. **21**, 918). γ-iso*Propylbutyrolactone*, $(CH_3)_2CH{\cdot}CHCH_2CH_2COO$, b.p. 224°, is formed from *iso*propylparaconic acid. α- and β-iso*Propylbutyrolactone* are obtained from *iso*propylsuccinic anhydride. *ααγ-Trimethylbutyrolactone, α-dimethylvalero-γ-lactone*, $CH_3{\cdot}CH{\cdot}CH_2C(CH_3)_2COO$, m.p. 52°, b.p. 86°/15 mm., may be obtained from α-dimethyllævulinic acid (mesitonic acid (*q.v.*)) and from ααγ-trimethylvinylacetic acid (C. 1904, I. 720). *αγγ-Trimethylbutyrolactone*, m.p. 50°, is prepared from αγγ-trimethyl-β-hydroxybutyric acid (comp. p. 423) (C. 1897, II. 572). *α-Ethyl-γ-methylbutyrolactone*, b.p. 219°, is prepared from α-ethyl-β-acetopropionic acid and ethylallylacetic acid, mode of formation, No. 3 (Ber. **29**, 1857). *γγ-Methylethylbutyrolactone*, b.p. 106°/18 mm., is obtained from lævulinic ester and ethyl magnesium halides.

Lactones : $C_8H_{14}O_2$. γ-iso*Butylbutyrolactone* is prepared from *iso*-butylparaconic acid. *γ-Methyl-α-propylbutyrolactone*, b.p. 233°. *γ-Methyl*-α-iso*propylbutyrolactone*, b.p. 224° (Ber. **29**, 1857, 2001). βγ-Dimethyl-α-ethylbutyrolactone, b.p. 227°, is obtained from α-ethyl-β-methyl-β-acetopropionic acid. *γ-Diethylbutyrolactone*, b.p. 228–233°, is prepared from succinyl chloride and zinc ethyl.

δ-Lactones

δ-Lactones are obtained by distillation of the δ-halogencarboxylic acids, or by reduction of the δ-ketocarboxylic acids (p. 480), glutaric esters or glutaric anhydrides (p. 557). They are also obtained by an intramolecular Cannizarro reaction from the easily accessible derivatives of glutaric aldehyde (p. 400) by means of sodium ethoxide (yields up to 90%) (*Meerwein*, Ber. **53**, 1829) :

$$\begin{array}{l} CHEt{\cdot}CHMe{\cdot}CHO \\ | \\ CMe_2{\cdot}CHO \end{array} \longrightarrow \begin{array}{l} CHEt{\cdot}CHMe{\cdot}CH_2. \\ |\qquad\qquad\qquad\; | \\ CMe_2{\cdot}CO\text{——}O \end{array}$$

δ-Valerolactone, $CH_2CH_2CH_2CH_2COO$, b.p. 114°/14 mm., changes spontaneously into a *polymer*, m.p. 48°, which is decomposed by alkali into δ-hydroxyvaleric acid, as is also the simple lactone (Ber. **26**, 2574 : **36**, 1200 : Ann. **319**, 367).

δ-Caprolactone, δ-methyl-δ-valerolactone, $C_6H_{10}O_2$, m.p. 13°, b.p. 275°. α- or *γ-Methyl-δ-valerolactone* (Ber. **36**, 1201).

αα-Dimethyl-δ-valerolactone, $C_7H_{12}O_2$, b.p. 105°/15 mm. *ββ-Dimethyl-δ-valerolactone*, m.p. 30°, b.p. 225° (C. 1905, II. 753).

δ-Methyl-γ-ethyl-δ-valerolactone, b.p. 255° (Ann. **216**, 127 : **268**, 117).

Higher Lactones and Carboxylic Acids

ε-Hydroxy-carboxylic acids and hydroxy-acids containing a still more remote position of the alcoholic OH-group show no further tendency to lactone-formation. They seem rather to split off water like the β-hydroxy-acids, since olefine carboxylic acids are obtained from the corresponding amino-carboxylic acids with nitrous acid, together with or instead of the hydroxy-acids (Ann. **343**, 44).

However, ε-**Lactones** have been obtained by the oxidation of certain terpene ketones with permonosulphuric acid (Caro's acid). *β-Methyl-ε*-iso*propyl-ε-caprolactone*, $C_3H_7CHCH_2CH_2CH(CH_3)CH_2COO$, b.p. 129°/17 mm., two stereoisomerides, m.p. 4·8° and 47°. It is obtained from menthone (Vol. II). The two isomers yield *hydroxy-acids*, one liquid and the other, m.p. 65° ; but only one ε-keto-acid is obtained by oxidation.

Tetrahydrocarvone (Vol. II) similarly treated yields *ε-methyl-β*-iso*propyl-ε-caprolactone*, b.p. 156°/21 mm.

Methyl*cyclo*hexanone (Vol. II) gives rise to a lactone, which, on breaking down, passes into methyl-ε-hydroxycaproic acid. Suberone (Vol. II) appears to give a ζ-lactone which passes into ζ-hydroxyœnanthylic acid, $HOCH_2[CH_2]_5{\cdot}COOH$, on decomposition (Ber. **33**, 858).

ε-Hydroxycaproic acid, $HO[CH_2]_5{\cdot}COOH$; *phenyl ether*, $C_6H_5O[CH_2]_5COOH$, m.p. 71°, is obtained by adding potassium cyanide to ε-chloroamyl phenyl ether and hydrolysing the resulting nitrile (Ber. **38**, 965).

κ-Hydroxyundecoic, $HOCH_2[CH_2]_9COOH$, m.p. 70°, is obtained from ω-bromoundecylic acid and silver oxide. Oxidation converts it into nonane dicarboxylic acid (C. 1901, II. 1043).

ι-Hydroxystearic acid, $C_8H_{17}CH(OH)[CH_2]_8COOH$, m.p. 83°, is produced from oleic acid through iodo- or sulphostearic acid (*cf.* p. 431). If oleic acid is heated with zinc chloride it is converted into the so-called *stearolactone*, $C_{18}H_{32}O_2$, probably γ-tetradecylbutyrolactone (C. 1903, I. 1404).

ν-Hydroxybehenic acid, $C_8H_{17}{\cdot}CH(OH)C_{12}H_{24}COOH$, m.p. 90° (C. 1908, I. 2019).

Higher lactones occur in the vegetable musks. Thus the lactone of ω-hydroxypentadecoic acid occurs in angelica oil (Ber. **60**, 902 : *cf.* also Ambrettolide, p. 454).

Sulphur Derivatives of the Hydroxy-acids

The mercaptan carboxylic acids and their derivatives will be considered here. These are acids which at the same time possess the nature of a mercaptan. They are obtained as oils, with a disagreeable odour, and are miscible with water, alcohol, and ether.

1. **Mercaptan carboxylic acids** are prepared (1) from halogen-fatty acids and KSH ; (2) the xanthogen-fatty acids resulting from potassium xanthogenate (*q.v.*) and chloro-fatty acids, are decomposed by ammonia into mercaptan-carboxylic acid and xanthogen amide (Ber. **39**, 732 : Ann. **348**, 120) :

$$ClCH_2COOK + KSH = HSCH_2COOK + KCl$$
$$C_2H_5OCS{\cdot}SCH(CH_3)COONH_4 + NH_3 = HSCH(CH_3)COONH_4 + C_2H_5OCS{\cdot}NH_2.$$

(3) The mercaptan- or thio-carboxylic acids are easily oxidized to *disulphides*, such as $(HOOCCH_2)_2S_2$, which may also be prepared directly from halogen-fatty acids and potassium polysulphides ; on reduction, the mercaptan carboxylic acids are re-formed (C. 1907, I. 856 : 1908, I. 1221).

These bodies tend to form complex salts.

Thioglycollic acid, *thiolacetic acid*, $HS{\cdot}CH_2COOH$, m.p. − 16·5°, b.p. 103°/13 mm., is obtained from monochloroacetic acid and potassium hydrogen sulphide ; and from thiohydantoin, when heated with alkalis (Ann. **207**, 124). On adding ferric chloride to its solution an indigo-blue coloration is obtained. It is a dibasic acid. (Conductivity, Ber. **39**, 736.) The *barium salt*, $\overline{S{\cdot}CH_2COOBa}$ + $3H_2O$, dissolves with difficulty in water ; *ethyl ester*, b.p. 55°/17 mm. ; *amide*, m.p. 52°. On being heated, thioglycollic acid yields *thioglycollide* $(SCH_2CO)_x$, m.p. about 80°.

Thiolactic acid, *α-thiolpropionic acid*, $CH_3CH(SH)CO_2H$, m.p. 10°, b.p. 99°/14 mm., is prepared from pyroracemic acid (p. 462) and sulphuretted hydrogen ; also, together with cysteine, α-amino-β-thiopropionic acid (*q.v.*) (C. 1903, I. 15), from horn (keratin) by decomposition with hydrochloric acid. *β-Thiolpropionic acid*, $HS{\cdot}CH_2CH_2CO_2H$, m.p. 16·8°, b.p. 11°/15 mm., $D_{20} = 1{\cdot}218$.

α-Thiolbutyric acid, b.p. 118–122°/19 mm. ; *α-thiol*iso*butyric acid*, m.p. about 47°, b.p. 102°/15 mm. Reaction between *γ-chlorobutyronitrile* and potassium hydrosulphide, see Ber. **34**, 3387.

2. **α-Alkyl sulphide carboxylic acids** are obtained from the interaction of α-halogen fatty acids and sodium mercaptides.

Ethylthiolacetic acid, $C_2H_5S{\cdot}CH_2COOH$, m.p. −8·7°, b.p. 118°/11 mm. ; $D_{20} = 1{\cdot}1518$ (Ber. **40**, 2588).

3. **α-Mercaptal carboxylic acids** result from the action of α-thio-acids on aldehydes. *Ethylidenedithioglycollic acid*, $CH_3CH : (SCH_2{\cdot}COOH)_2$, m.p. 107°.

4. **α-Mercaptole carboxylic acids** result from α-thio-acids and ketones in the presence of zinc chloride or HCl.

iso*Propylidenedithioglycollic acid*, $(CH_3)_2C : (SCH_2COOH)_2$, m.p. 126°.

5. **α-Sulphide dicarboxylic acids** are produced when K_2S acts on α-halogen fatty acids.

Thiodiglycollic acid, $S(CH_2CO_2H)_2$, m.p. 129°, corresponds with diglycollic acid (p. 420), and under like conditions forms a cyclic anhydride, which is both a sulphide and a carboxylic anhydride. *Thiodiglycollic anhydride*, $S<\begin{matrix}CH_2CO\\CH_2CO\end{matrix}>O$, m.p. 102°, b.p. 158°/10 mm. (Ber. **27**, 3059).

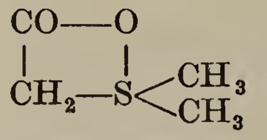
α-Thiodilactylic acid, $S[CH(CH_3)CO_2H]_2$, m.p. 125°. *γ-Thiodibutyric acid*, m.p. 99° (Ber. **25**, 3040).

unsym.-*Sulphide dicarboxylic acids* are obtained from the disodium salts of the mercaptan carboxylic acids and sodium halogen fatty acids in aqueous solution (Ber. **29**, 1139).

6. **Disulphide dicarboxylic acids** are readily produced by the oxidation of the mercaptan carboxylic acids in the air, or with ferric chloride or iodine. *Dithiodiglycollic acid*, $S_2(CH_2CO_2H)_2$, m.p. 100°. *α-Dithiodilactic acid*, $S_2[CH(CH_3)\cdot CO_2H]_2$, m.p. 141°. *β-Dithiodipropionic acid*, $S_2(CH_2CH_2COOH)_2$, m.p. 155° (Ann. **339**, 351).

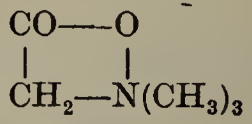
Trithiodiacetic acid, $S_3(CH_2COOH)_2$, m.p. 124°. *Tetrathiodiacetic acid*, $S_4(CH_2COOH)_2$, m.p. 113° (Ann. **359**, 81).

7. **Sulphonium Derivatives of Carboxylic Acids.**—The free bodies—*e.g.* $\begin{matrix}COOH\\|\\CH_2S(CH_3)_2OH,\end{matrix}$ are unstable. They split off water and yield cyclic sulphinates, which are constituted similarly to the cyclic ammonium compounds, and are called thetines. This name, from the contraction of thio and betaine, is intended to express the analogy between their derivatives and betaine (Ber. **7**, 695 : **25**, 2450 : **26**, R. 409) :



$$\begin{matrix}CO\text{—}O\\|\quad\;\;|\\CH_2\text{—}S<\begin{matrix}CH_3\\CH_3\end{matrix}\end{matrix}$$

Dimethylthetine.



$$\begin{matrix}CO\text{—}O\\|\quad\;\;|\\CH_2\text{—}N(CH_3)_3\end{matrix}$$

Betaine.

The thetines are feeble bases. Their hydrobromides are produced when methyl sulphide, ethyl sulphide, and sodium thiodiglycollate are brought into action with α-halogen fatty acids—*e.g.* chloroacetic acid and α-bromopropionic acid.

Dimethylthetine, $(CH_3)_2\overline{SCH_2COO}$, is deliquescent.

Methylethylthetine, $\begin{matrix}CH_3\\C_2H_5\end{matrix}>\overset{*}{S}<\begin{matrix}CH_2\\O\end{matrix}>CO$, contains an asymmetric sulphur atom, and is resolved into its two forms by means of its salts with camphor-sulphonic acid and bromocamphor-sulphonic acid : d-*chloroplatinate*, $[\alpha]_D = +4{\cdot}5°$ (C. 1900, II. 623).

Dimethylthetinedicarboxylic acid, $(HO\cdot OC\cdot CH_2)_2\overline{S\cdot CH_2\cdot COO}$, m.p. 157–158°. *Diethylenedisulphidethetine* (C. 1899, II. 1105). Further compounds, Ber. **33**, 823.

Selenetines, see Ber. **27**, R. 801 : C. 1903, I. 22.

8. **Sulphone carboxylic acids** are produced by the action of alkyl sulphinates on esters of halogen fatty acids, and resemble the ketone carboxylic acids (*q.v.*). *Ethylsulphonylacetic acid*, $C_2H_5SO_2\cdot CH_2CO_2H$. *Ethylsulphonylpropionic acid*, $C_2H_5SO_2\cdot CH_2CH_2CO_2H$ (Ber. **21**, 89, 992).

By oxidizing the sulphide, corresponding with the sulphones, with $KMnO_4$, there are obtained : *Sulphonyldiacetic acid*, $O_2S(CH_2CO_2H)_2$, m.p. 182°. *α-Sulphonyldipropionic acid*, $O_2S[CH(CH_3)\cdot CO_2H]_2$, m.p. 155° (Ber. **18**, 3241). Sulphone diacetic acid resembles acetoacetic ester in many respects. For mixed sulphone-di-fatty acids see Ber. **29**, 1141.

9. α-**Sulphocarboxylic acids.** The sulpho-acids of the fatty acids are produced by methods similar to those employed with the alkyl sulphonic acids :

(1) By the action of sulphur trioxide on the fatty acids, or by acting with fuming sulphuric acid on the anhydrides, nitriles, or amides of the acids (J. pr. Chem. [2] 73, 538 : C. 1905, I. 1309).

(2) By heating the salts of the monosubstituted fatty acids with alkali sulphites.

(3) By the addition of alkali sulphites to unsaturated acids (Ber. **18**, 483).

(4) By oxidizing the thio-hydroxy-acids with nitric acid.

(5) By oxidizing sulphonic acids, *e.g.* isethionic acid, with nitric acid.

The sulpho-acids are dibasic acids, corresponding with malonic acid in their chemical behaviour. They are, however, more stable towards heat, alkalis, and acids.

Sulphoacetic acid, $HO{\cdot}SO_2{\cdot}CH_2{\cdot}COOH$, is formed together with methionic acid, $CH_2(SO_3H)_2$ (p. 247), by decomposition of acetonetrisulphonic acid, $HO{\cdot}SO_2{\cdot}CH_2{\cdot}CO{\cdot}CH(SO_3H)_2$, by means of alkali (C. 1901, I. 101). (See also acetylsulphuric acid, p. 317.) Its *dichloride*, $Cl{\cdot}SO_2{\cdot}CH_2{\cdot}COCl$, b.p. 130–135°/150 mm., yields thioglycollic acid on reduction. The hydrogen atoms in the CH_2 group of the *diethyl ester*, $EtO{\cdot}SO_2{\cdot}CH_2{\cdot}COOEt$ (an oil which cannot be distilled without decomposition), can be replaced by alkyl groups, similarly to those in methionic esters, acetoacetic ester and malonic ester (Ber. **21**, 1550).

Sulpho*iso*butyric acid, $HO_3S{\cdot}C(CH_3)_2COOH$, is formed by the interaction of *iso*butyryl chloride or anhydride and concentrated sulphuric acid. The *barium salt* ($+ 3H_2O$) is less easily soluble in hot water than in cold ; *dimethyl ester*, m.p. 4°, b.p. 78–82°/1 mm. ; *dichloride*, m.p. — 10°, b.p. 55°/1 mm. (C. 1905, I. 1309).

Nitrogen Derivatives of the Hydroxy-acids

The following classes of nitrogen compounds are derived from the α-hydroxy-acids : (A) *Derivatives formed by modification of the* COOH *group :* (1) Amides. (2) Imidohydrins. (3) Hydrazides. (4) Azides. (5) Nitriles. (B) *Derivatives formed by substitution of the* ·OH *group :* (6) Nitro-acids. (7) Nitroso-acids. (8) Hydroxylamino-acids. (9) Aminoxyl-acids. (10) Amino-acids. (11) Nitroamino-acids. (12) *iso*-Nitroamino-acids. (13*a*) Hydrazino-acids. (13*b*) Hydrazo-acids. (14) Azo-acids.

The α-amino-acids and their derivatives are of especial interest from the physiological standpoint, as being decomposition products of the proteins.

(A) *Derivatives formed by Modification of the* COOH *Group*

1. **Hydroxyamides.**—The α-hydroxyamides are produced (1) by treating (*a*) alkyl esters and (*b*) cyclic double esters or lactides with ammonia. (2) From the α-hydroxynitriles by the addition of water in the presence of a mineral acid, particularly sulphuric acid. They behave like the fatty acid amides.

Glycollamide, $HOCH_2CO{\cdot}NH_2$, m.p. 120°, is obtained from polyglycollide, or from acid ammonium tartronate when heated to 150°. It possesses a sweet taste.

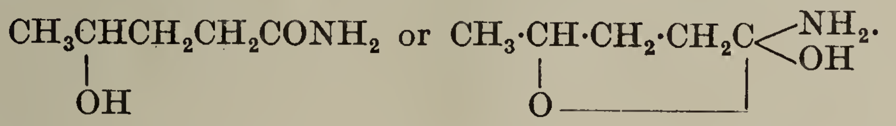
Diglycollamic acid, $NH_2COCH_2OCH_2CO_2H$, m.p. 135°.

Diglycollamide, $O(CH_2CONH_2)_2$, breaks down when heated into ammonia and *diglycollimide,* $O\!<\!\begin{smallmatrix}CH_2{\cdot}CO\\CH_2{\cdot}CO\end{smallmatrix}\!>\!NH$, m.p. 142°. It behaves like the imides of the dicarboxylic acids, *e.g.* succinimide (*q.v.*) and *n*-glutarimide.

Lactamide, $CH_3CH(OH){\cdot}CONH_2$, m.p. 74°.

α-Hydroxycaprylamide, $CH_3(CH_2)_5CH(OH)CONH_2$, m.p. 150° (Ann. **177**, 108).

The readily decomposable additive products from ammonia and the γ-lactones (Ann. **256**, 147), are regarded as being as γ-hydroxy-acid amides or as compounds similarly constituted to aldehyde-ammonia (Ann. **259**, 143). The additive product from ammonia and γ-valerolactone may be formulated :



$$\underset{\displaystyle OH}{CH_3\underset{|}{C}HCH_2CH_2CONH_2} \quad \text{or} \quad CH_3{\cdot}\underbrace{\overset{}{CH}{\cdot}CH_2{\cdot}CH_2C}_{O}\!<\!\begin{smallmatrix}NH_2\\OH\end{smallmatrix}.$$

The addition products of hydrazine and γ-lactones behave similarly : *Hydrazine γ-valerolactone,* $\overbrace{O{\cdot}CH(CH_3)CH_2CH_2C}(OH)(NM{\cdot}NH_2)$, m.p. 62°, also easily dissociates into hydrazine and lactone (C. 1905, I. 1221).

2. **α-Hydroxy-imidohydrins.** The *imido-ethers* of the α-hydroxy-acids, whose salts are prepared in the ordinary way from nitriles by means of alcohols

and HCl (p. 326), are hydrolysed when in the free state by water, into the *imidohydrins.* These are isomeric with the corresponding amides, although they appear to consist of a double molecule and behave as electrolytes in aqueous solution (Ber. **30**, 998 : **34**, 3142).

Glycoliminohydrin, $\left(HOCH_2C{<}^{NH}_{OH}\right)_2$, m.p. 160° ; *lactimidohydrin,* m.p. 135° ; *hydroxy*iso*butyl imidohydrin,* m.p. 173°.

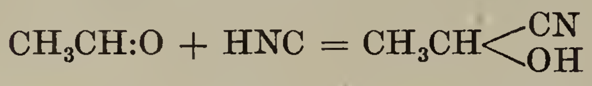
3. **Hydrazides of the hydroxy-acids :** *Glycollyl hydrazide,* $HOCH_2CO{\cdot}NHNH_2$, m.p. 93°, has been prepared from benzoyl or oxalyl glycollic ester and hydrazine hydrate (J. pr. Chem. [2], **51**, 365).

4. **Azides of the hydroxy-acids :** *Glycollyl azide,* $HOCH_2{\cdot}CON_3$, is formed when sodium nitrite acts on the hydrochloride of glycollyl hydrazide. It crystallizes from ether (J. pr. Chem. [2], **52**, 225).

5. **Nitriles of the Hydroxy-acids.**—The nitriles of the α-hydroxy-acids are the additive products obtained from hydrocyanic acid and the aldehydes or ketones, usually known as *cyanohydrins.*

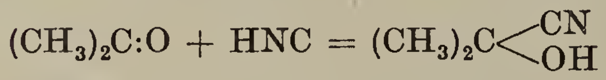
The *aldehydes* yield nitriles of *secondary* hydroxy-acids. Formaldehyde is an exception in this respect, for it gives rise to the nitrile of a primary hydroxy-acid,—glycollic acid.

The *ketones* yield nitriles of *tertiary* hydroxy-acids.



$$CH_3CH{:}O + HNC = CH_3CH{<}^{CN}_{OH}$$

Nitrile of lactic acid (p. 415).



$$(CH_3)_2C{:}O + HNC = (CH_3)_2C{<}^{CN}_{OH}$$

Nitrile of α-hydroxy*iso*butyric acid (p. 423).

The cyanohydrins result by the reaction of the aldehyde and ketone bisulphite compounds (pp. 244, 266) with potassium cyanide (Ber. **38**, 214 : **39**, 1224, 1856).

Many of the anhydrous substances boil without decomposition, especially under reduced pressure ; but many break down upon the evaporation of their aqueous solution, and alkalis resolve them into their components. On the other hand, under the influence of mineral acids, *e.g.* hydrochloric acid and sulphuric acid, the nitriles first take up one molecule of water and change to α-hydroxy-acid amides (see above), then a second molecule of water, and form the ammonium salts of the α-hydroxy-acids, which are immediately decomposed by mineral acids (p. 322).

When heated with P_2O_5 they change into olefine carboxylic nitriles ; with PCl_5 into chloroparaffin carboxylic nitriles (C. 1898, II. 22, 662). Ammonia causes the formation of water and amino-nitriles (p. 435). Cyanoacetic ester and the α-hydroxy-acid nitriles produce water and derivatives of αβ-dicyanopropionic acids, $R_2C(CN){\cdot}CH(CN)CO_2C_2H_5$ (C. 1906, II. 1561).

Aldehyde Cyanohydrins.

Glycollic acid nitrile, $HO{\cdot}CH_2CN$, b.p. 183° with decomposition, b.p. 103°/26 mm. (J. pr. Chem. [2] **25**, 189). *Acyl glycollic nitriles* are prepared from chloroacetic nitrile with the sodium or potassium salts of the fatty acids (C. 1904, II. 1377). *Formoxyacetonitrile,* HCO_2CH_2CN, b.p. 173°, and *acetoxyacetonitrile,* b.p. 180°, result also from glycollaldoxime and acetic anhydride, and are decomposed by ammoniacal silver oxide into AgCN and formaldehyde (C. 1900, II. 313). *Ethers* of glycollic nitrile are prepared from chloromethyl alkyl ethers and silver, mercury, or copper cyanide : *Methoxyacetonitrile,* b.p. 120° ; *ethoxyacetonitrile,* b.p. 135° (C. 1907, I. 400, 871).

Lactic acid nitrile, *aldehyde cyanohydrin,* $CH_3CH(OH)CN$, b.p. 102°/30 mm.; *ethyl ether,* $CH_3CH(OC_2H_5)CN$, b.p. 88°, is prepared from cyanogen chloride and ethyl ether (Ber. **28**, R. 15); *acetyl ester*, $CH_3CH(OCOCH_3)CN$, b.p. 169° (Ber. **28**, R. 109).

α-Hydroxy*iso*valeric acid nitrile, $(CH_3)_2CH{\cdot}CH(OH)CN$, decomposes at 135°.

Halogen Substitution Products of the Aldehyde Cyanohydrins (Ann. **179**, 73): *Chloral cyanohydrin*, $CCl_3CH(OH)CN$, m.p. 61°, boils with decomposition at 215–230°. *Tribromolactic acid nitrile*, $CBr_3CH(OH)CN$. Both compounds can also be looked on as trihalides of orthotartronic acid nitriles. *Trichlorovalerolactic acid nitrile*, $CH_3CCl_2CHCl{\cdot}CH(OH)CN$, m.p. 103°.

Ketone Cyanohydrins: *α-Hydroxy*iso*butyric nitrile, acetone cyanohydrin*, $(CH_3)_2C(OH)CN$, m.p. − 19°, b.p. 82°/23 mm.

Methylethylglycollic nitrile, $(C_2H_5)(CH_3){\cdot}C(OH)CN$, b.p. 91°/20 mm.

Diethylglycollic nitrile, $(C_2H_5)_2{\cdot}C(OH)CN$, b.p. 110°/22 mm.

*β-Chloro-α-hydroxy*iso*butyric nitrile*, $ClCH_2C(CH_3)(OH)CN$, m.p. 110°/22 mm.

*Methyl-*tert.*-butylglycollic nitrile*, $(CH_3)_3CC(CH_3){\cdot}(OH)CN$, m.p. 94°, is prepared from pinacolin (Ann. **204**, 18: Ber. **14**, 1974: **39**, 1858: C. 1906, II. 596).

Nitriles of other hydroxy-acids have been prepared from the halogen glycolhydrins (p. 369) by the action of potassium cyanide. *Ethylene cyanohydrin, hydracrylic nitrile*, $HOCH_2CH_2CN$, b.p. 220°, is also obtained from ethylene oxide and hydrocyanic acid. *β-Ethoxybutyronitrile*, $CH_3CH(OC_2H_5)CH_2CN$, b.p. 173°, is prepared from allyl cyanide and ethyl alcohol (Ber. **29**, 1425). *γ-Methoxybutyronitrile*, $CH_3O[CH_2]_3{\cdot}CN$, b.p. 173° (Ber. **32**, 948).

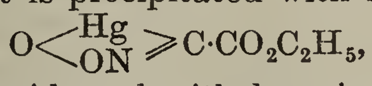
ε-Phenoxycapronitrile, $C_6H_5O[CH_2]_5{\cdot}CN$, m.p. 36°, from ε-chlorocapronitrile and sodium phenate (Ber. **38**, 178).

(B) *Derivatives formed by Substitution of the* ·OH *Group*

6. **Nitro-fatty acids.** *α-Nitro-fatty acids* are only known in the form of derivatives. When potassium nitrite acts on potassium chloroacetate there is first formed potassium nitro-acetate which decomposes into nitromethane and potassium bicarbonate (*cf.* p. 179):

$$CH_2ClCOOK \xrightarrow{KNO_2} NO_2CH_2CO_2K \xrightarrow{H_2O} CH_3NO_2 + KHCO_3.$$

When silver nitrite and bromoacetic ester react, the expected nitro-acetic ester is replaced by two peculiar bodies containing less water, which are derivatives of oxalic acid: *oxalic ester nitrile oxide*, $C_2H_5OCO{\cdot}C \vdots N : O$, m.p. 111°, and *bis-anhydro-nitro-acetic ester*, $(C_2H_5OCOCNO)_2$, b.p. 160°/11 mm., which on reduction yields glycine, like a true nitro-acetic ester. Similarly, iodo-acetonitrile and silver nitrite do not yield nitro-acetonitrile, but a dimolecular body, deficient in water, *cyanomethazonic acid*, which is possibly *iso*nitroso-nitro-succinonitrile, $NC{\cdot}C(:NOH){\cdot}C(:NOOH)CN$ (*cf.* methazonic acid, p. 391) (Ber. **34**, 870).

The real **nitro-acetic ester**, $NO_2{\cdot}CH_2{\cdot}COOC_2H_5$, b.p. 94°/10 mm., is prepared from nitromalonic ester, $NO_2CH(COOC_2H_5)_2$ and KOH; also from α-nitrodimethyl acrylic ester, $(CH_3)_2C : C(NO_2)COOC_2H_5$, by the decomposing action of ammonia; also, particularly easily, from acetoacetic ester by the action of concentrated nitric acid and acetic anhydride, together with bis-anhydro-nitro-acetic ester (see above) (C. 1904, II. 640). Reduction changes it to hydroxylamino-acetic acid and glycocoll (C. 1901, II. 1259: *cf.* I. 881). Like other nitro-bodies, nitro-acetic acid forms *aci*-nitro salts (p. 50), $MOON : CHCO_2C_2H_5$. When the ammonium salt is precipitated with mercuric chloride a very stable *mercury nitro-acetic ester*,  $O{<}\genfrac{}{}{0pt}{}{Hg}{ON}{\geqslant}C{\cdot}CO_2C_2H_5$, is formed, which is soluble in alkalis and hydrochloric acid, and with bromine forms *dibromonitroacetic ester*, $NO_2CBr_2CO_2C_2H_5$, b.p. 131–134°/11 mm. (Ber. **39**, 1956). Heating with ammonia at 100° converts it into *nitroacetamide*, $NO_2CH_2CONH_2$, m.p. 101–102°, with decomposition. This can also be formed by alkaline decomposition of nitro-malonamide. Its silver salt reacting with alkyl iodides give O-*ethers*, such as $CH_3OON : CHCONH_2$ which decompose readily into aldehydes and iso*nitroso-acetamide*, $HON : CHCONH_2$. *Dibromonitroacetamide*, $NO_2CBr_2CONH_2$, and *bromonitroacetamide*, $NO_2CHBrCONH_2$, m.p. 79° (C. 1906, I. 910: Ber. **37**, 4623). *Nitro-acetonitrile*, NO_2CH_2CN, b.p. 96°/14 mm., is prepared from methazonic acid (p. 391) and thionyl chloride. With bromine it gives *dibromonitroacetonitrile*, NO_2CBr_2CN, b.p. 58°/12 mm., which is a different body from dibromoglyoxime peroxide (p. 296) (Ber. **41**, 1044).

Homologous α-nitro-fatty esters, such as *α-nitropropionic ester*, $CH_3CH(NO_2)CO_2C_2H_5$, b.p. 190–195° ; *α-nitrobutyric ester*, $C_2H_5CH(NO_2)CO_2C_2H_5$, b.p. 123°/20 mm., are obtained from the alkyl-nitro-malonic esters and sodium alcoholate (C. 1904, II. 1600). *α-Nitro*-iso*butyric acid*, $(CH_3)_2C(NO_2)COOH$: *nitrile*, m.p. 53°, is obtained by oxidation of nitroso-*iso*butyric nitrile (below) with nitric acid ; *amide*, m.p. 118°.

β-Nitro-fatty acids : *β-Nitropropionic acid*, $NO_2CH_2CH_2CO_2H$, m.p. 66°, is prepared from β-iodopropionic and silver nitrite ; *ethyl ester*, b.p. 161–165°. *β-Nitro*-isovaleric *acid*, $(CH_3)_2C(NO_2){\cdot}CH_2CO_2H$, is obtained together with *ββ-dinitropropane*, $(CH_3)_2C(NO_2)_2$, by the action of nitric acid on *iso*valeric acid (Ber. **15**, 2324).

7. **Nitroso-fatty acids.** Nitroso-fatty acids, which contain the group $—CH_2{\cdot}NO$ or $=CH{\cdot}NO$, are tautomeric with the *iso*nitroso- or oximino-fatty acids, which will be considered later as derivatives of the aldehyde- and ketone-carboxylic acids (pp. 460, 465).

Oxidation by chlorine of hydroxyl-amino-*iso*butyric nitrile (see below) yields the nitrile of *nitroso*iso*butyric acid*, $(CH_3)_2C(NO)COOH$. The *nitrile* melts at 53° to a blue liquid ; *amide*, m.p. 158° (decomp.) ; *ester*, m.p. 89° ; *amidine*, $(CH_3)_2C(NO)C(NH)NH_2$, is converted by hydrocyanic acid, etc., into a series of peculiar bases (Ber. **34**, 1863 : **36**, 1283).

8. **Hydroxylamino-fatty acids.** Their nitriles result from the combination of hydrocyanic acid with aldoximes and ketoximes (p. 250) (Ber. **29**, 65). *Hydroxylaminoacetic acid*, $HONH{\cdot}CH_2COOH$, m.p. 132°, is obtained from *iso*nitroaminoacetic acid (p. 452) and from nitro-acetic ester (see above), also from *iso*benzaldoxime acetic acid (Vol. II) (Ber. **29**, 667).

α-Hydroxylaminobutyric acid, $CH_3{\cdot}CH_2CH(NHOH)COOH$, decomposes at 166° ; *nitrile*, m.p. 86°, results from propionaldoxime and HCN (Ber. **26**, 1548). *α-Hydroxylamino*iso*butyric acid*, $(CH_3)_2C(NHOH)COOH$, is prepared from *iso*nitroamino*iso*butyric acid (p. 452) ; *nitrile*, m.p. 98°, is produced from acetoxime and HCN ; further derivatives, see Ber. **34**, 1863.

9. **Aminoxyl-fatty acids** are isomeric with the hydroxylamino-fatty acids. *Aminoxyl-acetic acid*, NH_2OCH_2COOH, is obtained by the breaking down of ethyl benzhydroxime acetic acid, $C_6H_5C(OC_2H_5):NOCH_2COOH$. *Homologues*, see Ber. **29**, 2654.

10. Amino-fatty Acids

The *amino-fatty acids* are amino-derivatives of the monobasic fatty acids, produced by the replacement of one hydrogen atom in the latter by the amino-group :

$CH_3{\cdot}CO{\cdot}OH$ — Acetic acid.

$NH_2{\cdot}CH_2CO{\cdot}OH$ — Aminoacetic acid.

The firm union of the amino-group in them is a characteristic difference between these compounds and their isomeric acid amides. Boiling alkalis do not eliminate it, in which it resembles the NH_2 group of the amines. Several of these amino-acids occur already formed in plant and animal organisms, to which great physiological importance is attached. They can be obtained from proteins by heating the latter with hydrochloric acid, or alkalis, or by the action of ferments or bacteria.

The general methods in use for preparing the amino-acids are :

(1) The reaction of the monohalogen fatty acids when heated with ammonia (similar to the formation of the amines from the alkyl halides, p. 188) :

Thus chloroacetic acid yields

$NH_2{\cdot}CH_2{\cdot}COOH$ — Aminoacetic acid. (Glycine).

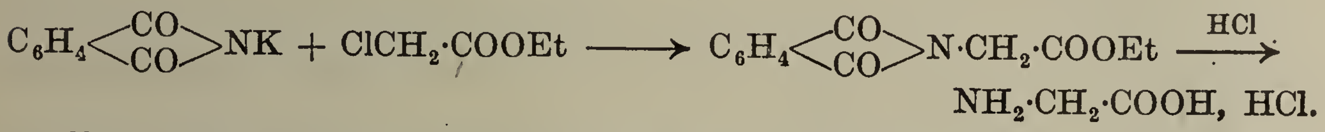
$NH(CH_2{\cdot}COOH)_2$ — Iminodiacetic acid. (Diglycollamic acid).

$N(CH_2{\cdot}COOH)_3$ — Triglycollamic acid.

Amino-acids with alkyl groups attached to the nitrogen are obtained from the monohalogen fatty acids or from hydroxy-acid nitriles by the action of amines (J. pr. Chem. [2] **65,** 188):

$$CH_2ClCOOH \xrightarrow{NH(CH_3)_2} CH_2<\begin{matrix}N(CH_3)_2\\COOH\end{matrix} \longleftarrow \begin{matrix}(CH_3)_2N\\NC\end{matrix}>CH_2 \xleftarrow{NH(CH_3)_2} \begin{matrix}HO\\NC\end{matrix}>CH_2.$$

(2) The replacement of the halogen in a halogen-fatty acid by the amino group is conveniently carried out by allowing the ester of the halogen acid to react with potassium phthalimide, the amino ester being subsequently split off by the action of hydrochloric acid at 200°:



$$C_6H_4<\begin{matrix}CO\\CO\end{matrix}>NK + ClCH_2\cdot COOEt \longrightarrow C_6H_4<\begin{matrix}CO\\CO\end{matrix}>N\cdot CH_2\cdot COOEt \xrightarrow{HCl} NH_2\cdot CH_2\cdot COOH,\ HCl.$$

Frequently the cheaper *p*-toluenesulphonamide can be used, and yields amino acids by reaction in aqueous or alcoholic solution with α-halogen-fatty acids (Z. angew. Chem. **39,** 1460).

(3) The reduction of nitro- and *iso*nitroso-acids (p. 433) with nascent hydrogen from zinc and hydrochloric acid or aluminium amalgam in ether (C. 1904, II. 1709):

$$CH_2NO_2COOC_2H_5 \xrightarrow{6H} CH_2NH_2COOH$$

Nitroacetic ester. Aminoacetic acid.

$$(CH_3)_2CHCH_2C(NOH)CO_2C_2H_5 \xrightarrow{4H} (CH_3)_2CHCH_2CH(NH_2)COOH$$

*iso*Nitroso*iso*butylacetic ester. *i*-Leucine (α-Amino*iso*caproic acid).

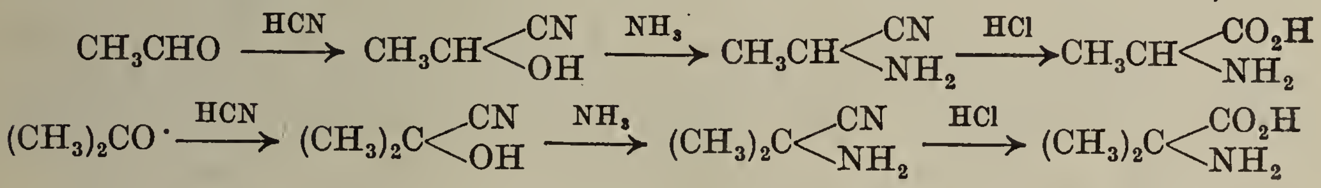
(4) Reaction of the cyano-fatty acids (*q.v.*) with nascent H (Zn and HCl, or by heating with HI), in the same manner that the amines are produced from the alkyl cyanides (p. 190):

$$CN\cdot COOH + 2H_2 = CH_2(NH_2)CO_2H$$

Cyanoformic acid. Aminoacetic acid.

This reaction connects the amino-fatty acids with the fatty acids containing an atom less of carbon, and also with the dicarboxylic acids of like carbon content, whose half nitriles are the cyano-fatty acids.

(5*a*) The nitriles of the α-amino-acids are prepared by allowing a calculated quantity of ammonia, in alcoholic solution, to act on the hydrocyanic acid addition-products of the aldehydes and ketones, and then setting free the hydrochlorides of the α-amino-acids from these by means of hydrochloric acid (Ber. **13,** 381: **14,** 1965):



$$CH_3CHO \xrightarrow{HCN} CH_3CH<\begin{matrix}CN\\OH\end{matrix} \xrightarrow{NH_3} CH_3CH<\begin{matrix}CN\\NH_2\end{matrix} \xrightarrow{HCl} CH_3CH<\begin{matrix}CO_2H\\NH_2\end{matrix}$$

$$(CH_3)_2CO \xrightarrow{HCN} (CH_3)_2C<\begin{matrix}CN\\OH\end{matrix} \xrightarrow{NH_3} (CH_3)_2C<\begin{matrix}CN\\NH_2\end{matrix} \xrightarrow{HCl} (CH_3)_2C<\begin{matrix}CO_2H\\NH_2\end{matrix}$$

(5*b*) Nitriles of α-amino-acids can also be synthetically obtained from the aldehyde-ammonias by means of hydrocyanic acid; also from aldehydes by means of ammonium cyanide (Ber. **14,** 2686):

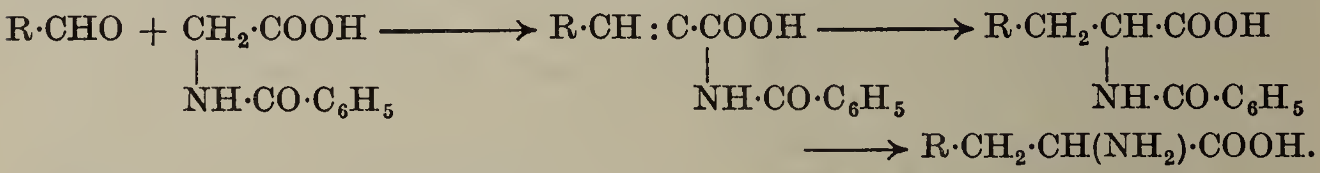
$$CH_3CH<\begin{matrix}OH\\NH_2\end{matrix} \xrightarrow{HCN} CH_3CH<\begin{matrix}CN\\NH_2\end{matrix} \xleftarrow{NH_4CN} CH_3CHO.$$

Ketones also unite with ammonium cyanide to form nitriles of the α-amino-dialkyl acetic acids (Ber. **33,** 1900: **39,** 1181).

Aldehydes and ketones may, with advantage, be allowed to act on a mixture of potassium cyanide and ammonium chloride (Ber. **39,** 1722).

Alkyl- and dialkylaminonitriles are obtained when aldehydes in bisulphite solution are treated with potassium cyanide and subsequently with primary or secondary amines (Ber. **38**, 213).

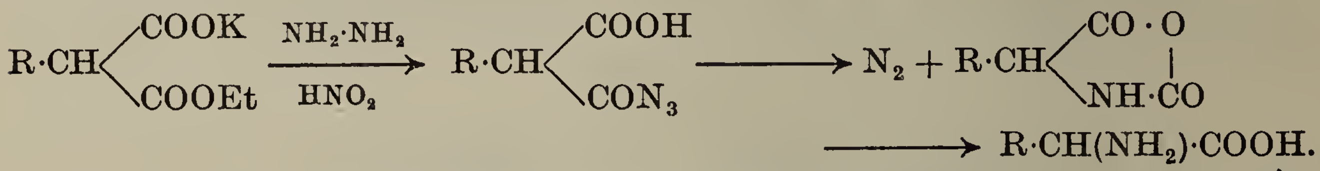
(6) Higher amino-acids can be synthesized by a reaction due to Erlenmeyer jun. (Ber. **30**, 2981 : Ann. **307**, 138). An aldehyde is condensed with hippuric acid (Benzoylglycine) and the product is reduced with sodium amalgam or hydriodic acid (D 1·7, Biochem. J. **21**, 852) and the benzoyl group hydrolysed off.



$$R{\cdot}CHO + \underset{NH{\cdot}CO{\cdot}C_6H_5}{CH_2{\cdot}COOH} \longrightarrow \underset{NH{\cdot}CO{\cdot}C_6H_5}{R{\cdot}CH{:}C{\cdot}COOH} \longrightarrow \underset{NH{\cdot}CO{\cdot}C_6H_5}{R{\cdot}CH_2{\cdot}CH{\cdot}COOH} \longrightarrow R{\cdot}CH_2{\cdot}CH(NH_2){\cdot}COOH.$$

Hydantoin is sometimes found more satisfactory than hippuric acid (Ber. **55**, 3859).

(7) Higher amino-acids can be obtained from the substituted malonic acids by converting these into the monoazides, heating the latter and hydrolysing the cyclic amidoanhydride with acids (Ber. **55**, 1543) :



(8) An important method of general application consists in the interaction of azoimide and substituted acetoacetic esters in benzene solution under the influence of strong sulphuric acid. The first-formed acetylamino ester yields the free amino-acid on hydrolysis (Ber. **57**, 704) :

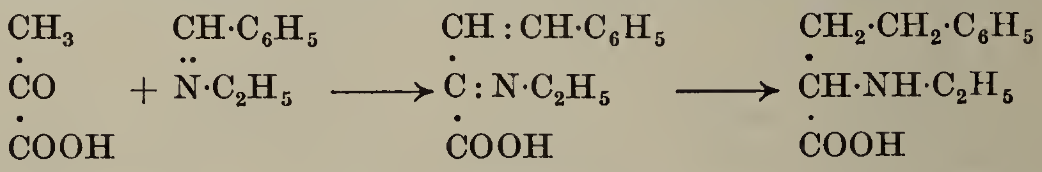
$$CH_3{\cdot}CO{\cdot}CHR{\cdot}COOEt + HN_3 \longrightarrow CH_3{\cdot}CO{\cdot}NH{\cdot}CHR{\cdot}COOEt + N_2$$
$$\longrightarrow CH_3{\cdot}COOH + NH_2{\cdot}CHR{\cdot}COOH + EtOH$$

(9) The formation of amino-acids by the catalytic hydrogenation of α-keto-acids in the presence of ammonia is of physiological importance. Imino-acids are probably intermediate products (Knoop, Z. physiol. Chem. **148**, 294) :

$$CH_3{\cdot}CO{\cdot}COOH + NH_3 \longrightarrow CH_3{\cdot}C({:}NH){\cdot}COOH \longrightarrow CH_3{\cdot}CH(NH_2){\cdot}COOH.$$

It is probable that amino-acids are formed by plants and animals in a similar manner. (For a different interpretation of the biological formation of amino-acids, see Bergmann, Z. physiol. Chem. **174**, 83.)

Skita has evolved a similar method for the preparation of alkylamino acids, *Schiff's bases* (p. 250) being condensed with pyruvic acid, usually with the formation of well-characterized condensation products, which are then hydrogenated with the use of platinum or palladium as catalysts (Ann. **453**, 190 : **455**, 17) :



$$\begin{array}{c}CH_3\\ \bullet\\ CO\\ \bullet\\ COOH\end{array} + \begin{array}{c}CH{\cdot}C_6H_5\\ \bullet\bullet\\ N{\cdot}C_2H_5\\ \\ \end{array} \longrightarrow \begin{array}{c}CH{:}CH{\cdot}C_6H_5\\ \bullet\\ C{:}N{\cdot}C_2H_5\\ \bullet\\ COOH\end{array} \longrightarrow \begin{array}{c}CH_2{\cdot}CH_2{\cdot}C_6H_5\\ \bullet\\ CH{\cdot}NH{\cdot}C_2H_5\\ \bullet\\ COOH\end{array}$$

Properties.—The amino-acids are crystalline compounds usually possessing a sweet taste. They are generally easily soluble in water, but usually very sparingly soluble in alcohol or ether.

Constitution.—The amino-acids contain both a carboxyl and an amino group, and hence show the properties of both acids and bases.

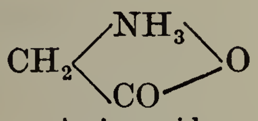
They react neutral, and it used to be considered that in neutral solution, both amino and carboxyl groups were practically undissociated. In alcoholic solution they react sufficiently acid to be filtrable with bases, using phenolphthalein as indicator (Ber. **54**, 2988). More recent views support the opposite view, that in neutral solution the compounds are practically completely dissociated, and possess what has been called a "*Zwitterion*" structure. The two formulæ can be represented as follows :

$NH_2{\cdot}CRR'{\cdot}COOH$ "*Classical*" formula.

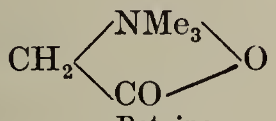
$NH_3^+{\cdot}CRR'{\cdot}COO^-$ "*Zwitterion*" formula.

The new formula is based on physico-chemical deductions from the relative acidic and basic strengths of the amino-acids and related compounds and on the titration curves of the amino-acids (see *Adams*, J.A.C.S. **38**, 1503 : *Bjerrum*, Z. physik. Chem. **104**, 147 : *Birch* and *Harris*, Biochem. J. **24**, 1080).

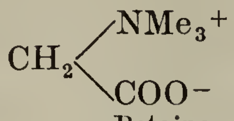
The acids were formerly represented as a cyclic ammonium salt on the analogy of betaine (and of the *β*- and *γ*-betaines, pp. 442, 448), but betaine itself may be represented by the dipole formula (Ber. **55**, 1762) :



Amino acid.
(*Cyclic* formula.)

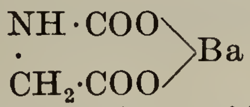


Betaine.



Betaine.
(Dipole formula.)

Reactions.—(1) The amino-acids form metallic salts by the action of bases.

(2) With acids, they form substituted ammonium salts. In the presence of alkalis or alkaline earths, the amino-acids combine with carbon dioxide to form the salts of a carbamino-carboxylic acid, the calcium or barium salt of which  $\begin{matrix} NH{\cdot}COO \\ \cdot \\ CH_2{\cdot}COO \end{matrix}\!\!>\!Ba$ is of value on account of its low solubility, in separating amino-acids from mixtures (Ber. **39**, 397 : Chem. Ztg. **1907**, 937). The difficultly soluble picrates and picrolonates are also of value in the separation of amino-acids.

Many amino-acids form compounds with neutral salts, see Z. physiol. Chem. **81**, 329.

(3) By the replacement of the carboxylic hydrogen by alkyl groups, esters are formed, which are very reactive compounds.

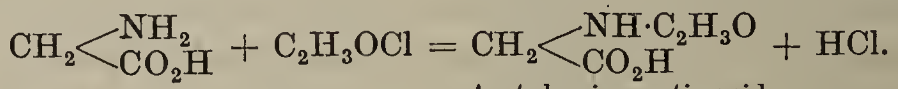
The esters are obtained as hydrochlorides by heating the acid with alcohol and hydrochloric acid. The free esters are compounds which can be distilled under diminished pressure without decomposition. They are liquids, with the properties of amines, fairly readily saponified. On heating they form diketopiperazines (p. 446).

The esters of the α-amino acids are of especial importance as the starting material for the preparation of the diazo-esters, and also for the separation of the amino-acids formed by the hydrolysis of proteins (Ber. **39**, 541).

(4) Phosphorus pentachloride converts the amino-acids, suspended in acetyl chloride, into hydrochlorides of the highly reactive *amino-acid chlorides* (*E. Fischer*, Ber. **38**, 2914) :

$$NH_2CH_2COOH + PCl_5 = HCl{\cdot}NH_2CH_2COCl + POCl_3.$$

(5) The hydrogen of the amino-group can also be replaced by acid and alcohol radicals. The *acyl* derivatives are obtained by the action of acid chlorides on an alkaline solution of the acid, or in presence of bicarbonate, or on the ester in a neutral solvent :



$$CH_2{<}\begin{matrix}NH_2\\CO_2H\end{matrix} + C_2H_3OCl = CH_2{<}\begin{matrix}NH\cdot C_2H_3O\\CO_2H\end{matrix} + HCl.$$

Acetylaminoacetic acid.

Those acyl derivatives which serve most suitably for identifying the amino-acids are the *benzoyl-*, *benzenesulphonic-*, and *naphthalenesulphonyl* compounds such as $C_6H_5\cdot CO\cdot NHCH_2COOH$, $C_6H_5SO_2\cdot NHCH_2COOH$, $C_{10}H_7SO_2\cdot NHCH_2\cdot COOH$. Another class of derivatives is the phenyl ureido-acids, such as $C_6H_5\cdot NHCONHCH_2COOH$, produced by phenyl *iso*cyanate (Vol. II) in alkaline solution (Ber. **35**, 3779 : **39**, 2359). The amino-group in the acyl amino-acids is " neutralized " by the acyl groups ; they are therefore stronger acids than the simple amino-acids, and many of them crystallize well.

Acyl groups can be introduced into the amino-acids by means of acid anhydrides and acid azides (J. pr. Chem. [2] **79**, 57). The formyl group can be introduced by the use of anhydrous formic acids (Ber. **38**, 3997). When α-amino-acids are heated with acetic anhydride and pyridine, carbon dioxide is lost and an α-acetamido-ketone produced (J. Biol. Chem. **78**, 91, 745) :

$$R\cdot CH(NH_2)\cdot COOH + (CH_3CO)_2O \longrightarrow R\cdot CH(NH\cdot CO\cdot CH_3)\cdot CO\cdot CH_3.$$

(6) The α-amino-acids react with formaldehyde to form compounds which contain three molecules of aldehyde to each molecule of acid. These compounds are converted into the simple *N*-methylene derivatives $R\cdot CH(\cdot N{:}CH_2)\cdot COOH$ by the action of alkali (Z. physiol. Chem. **131**, 18). These *N*-methylene compounds are of importance in the titration of amino-acids in the presence of formaldehyde by Sørensen's method, the influence of the amino-group being suppressed and the compounds reacting as acids (Biochem. Z. **7**, 45 : Z. physiol. Chem. **60**, 1).

The *barium* and *calcium* salts of the amino-acids react especially easily with aldehydes, with the formation of *N*-alkylidene derivatives (Ber. **58**, 1034).

(7) *Optical Resolution of Racemic Amino-acids.*—This is carried out by means of the strychnine, brucine, morphine, or cinchonine salts of the benzoyl- and formyl-amino acids. The resolution of racemic alanine, α-amino-butyric acid, α-amino-*iso*valeric acid, leucine, aspartic acid, and glutaminic acid, has been carried out in this manner (Ber. **32**, 2451 : **33**, 2370 : **38**, 3997) The resolution of the racemic synthetic α-amino-acids is of importance because it completes the laboratory production of the natural α-amino-acids (from proteins), which are all optically active. The resolution can also be carried out by the aid of yeasts, which consume either the *d*-form only, or only the *l*-form (C. 1906, II. 501).

(8) Exhaustive methylation (p. 198) causes the elimination of the amino-group, with the formation of unsaturated acids. Thus, α-aminopropionic acid yields acrylic acid ; α-aminobutyric acid gives rise to crotonic acid (Ber. **21**, R. 86) ; α-amino-*n*-valeric acid yields propylideneacetic acid (Ber. **26**, R. 937).

(9) Hydriodic acid at 200° causes the exchange of the amino-group for hydrogen, whereby the acid is converted into a fatty acid (Ber. **24**, R. 900).

(10) Boiling with alkalis does not affect the amino-acids, but fusion

with potassium hydroxide causes decomposition into ammonia or amines and salts of fatty acids.

(11) Dry distillation, especially in presence of barium oxide, decomposes the acids into amines and CO_2:

$$CH_3\cdot CH(NH_2)COOH = CH_3\cdot CH_2\cdot NH_2 + CO_2.$$

Aminoacetic acid. Ethylamine.

The same decomposition, with the formation of amines and carbon dioxide, is brought about by certain bacteria. The action of yeast on amino-acids is described on p. 141.

(12) The action of nitrous acid converts the amino-acids into hydroxy-acids, with evolution of nitrogen. This action, followed by the measurement of the evolved nitrogen, is the basis of Van Slyke's method for the estimation of amino compounds:

$$R\cdot CH(NH_2)\cdot COOH + HNO_2 \longrightarrow R\cdot CH(OH)\cdot COOH + N_2 + H_2O.$$

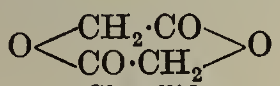
(13) The amino-ester hydrochlorides are changed by potassium nitrite into diazo-fatty esters (p. 458), the formation of which serves for the detection of small quantities of amino-acids (Ber. **17**, 959). In the presence of excess of hydrochloric acids, chloro-fatty acids are formed (C. 1901, I. 98). Similarly, nitrosyl bromide produces α-bromo-fatty acids.

(14) Ferric chloride produces a red coloration with all the amino-acids, which is destroyed by acids.

(15) Triketohydrindene hydrate (Vol. II) yields a blue colour which can be extracted with amyl alcohol, when heated with amino-acids. (*Ninhydrin* reaction: Constitution of the pigment, see J. Biol. Chem. **25**, 319: *cf.* Biochem. Z. **141**, 105.)

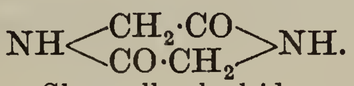
(16) The amino-esters can be reduced to amino-aldehydes (Ber. **41**, 956, 1019) and amino-alcohols (Helv. Chim. Acta. **4**, 76). Oxidation with hydrogen peroxide, see C. 1908, I. 1164.

(17) One of the chief characteristics of the α-amino-fatty acids is that when they lose water they yield cyclic double acid amides corresponding with the cyclic esters of the α-hydroxy-acids or lactides.



$$O\Big\langle\begin{matrix}CH_2\cdot CO\\ CO\cdot CH_2\end{matrix}\Big\rangle O$$

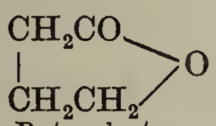
Glycollide.



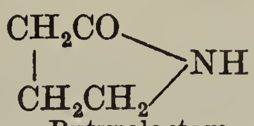
$$NH\Big\langle\begin{matrix}CH_2\cdot CO\\ CO\cdot CH_2\end{matrix}\Big\rangle NH.$$

Glycocoll anhydride.

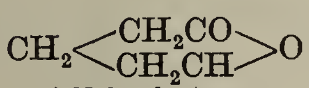
The γ- and δ-amino-acids, and amino-acids possessing long chains, however, are capable of forming cyclic, simple acid amides, the *lactams*, corresponding with the lactones, the cyclic, simple esters of the hydroxy-acids:



Butyrolactone.

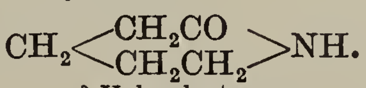


γ-Butyrolactam.
Pyrrolidone.



$$CH_2\Big\langle\begin{matrix}CH_2CO\\ CH_2CH_2\end{matrix}\Big\rangle O$$

δ-Valerolactone.



$$CH_2\Big\langle\begin{matrix}CH_2CO\\ CH_2CH_2\end{matrix}\Big\rangle NH.$$

δ-Valerolactam.
2-Piperidone.

Breakdown of α-Amino-acids in the Animal Organism. In contradistinction to the assumed β-oxidation of the fatty acids (see p. 308), the breakdown of the amino-acids starts at the α-carbon atom, probably by formation of an imino-acid, followed by deamination to an α-keto-acid, which is then decarboxylated and oxidized to the fatty acid containing one carbon atom less (*cf.* Synthesis, method (9), p. 436) (*Neubauer*, *Knoop*, Z. physiol Chem. **71**, 252):

$$R{\cdot}CH(NH_2){\cdot}COOH \longrightarrow R{\cdot}C(:NH){\cdot}COOH \xrightarrow{H_2O} R{\cdot}CO{\cdot}COOH + NH_3 \xrightarrow[O]{-\,CO_2} R{\cdot}COOH.$$

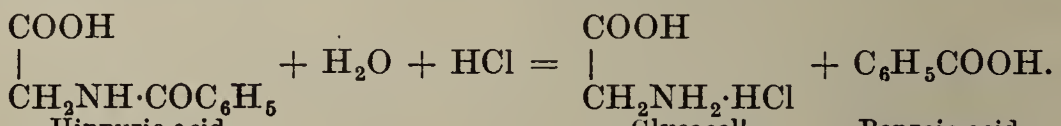
α-Amino-acids

Glycine, *glycocoll, aminoacetic acid,* $NH_2{\cdot}CH_2{\cdot}COOH$ (or $NH_3^+{\cdot}CH_2{\cdot}COO^-$, p. 437), m.p. 232–236°, is obtained by the general methods already described. It is obtained from chloroacetic acid by the action of ammonia or phthalimide, by the reduction of nitroacetic acid or cyanoformic acid, or by the hydrolysis of methyleneaminoacetonitrile, $CH_2:N{\cdot}CH_2{\cdot}CN$ (p. 441) with hydrochloric acid (J.C.S. **1929,** 2463) or of aminoacetonitrile, $NH_2{\cdot}CH_2{\cdot}CN$, with baryta. The last two and the first two methods are of practical importance. The preparation of the aminoacetonitrile and its conversion into glycine is as follows (Ann. **278,** 229: J. pr. Chem. [2] **65,** 188):

$$H{\cdot}CHO \xrightarrow{HCN} CH_2(OH){\cdot}CN \xrightarrow{NH_3} CH_2(NH_2){\cdot}CN \xrightarrow{Ba(OH)} CH_2(NH_2):COOH.$$

It is also obtained by the hydrolysis of hippuric acid (benzoylglycine), by the reduction of cyanogen gas by boiling hydriodic acid, by the action of ammonium cyanide and sulphuric acid on glyoxal, formaldehyde being a probable intermediate compound (Ber. **15,** 3087) and by the action of ammonia on glyoxylic acid, formylglycine being an intermediate (Ber. **35,** 2438).

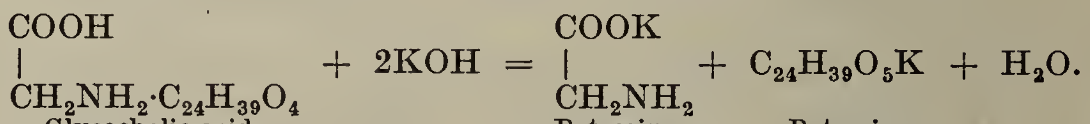
History.—*Braconnot* (1820) obtained glycocoll by decomposing glue with boiling sulphuric acid. It owes its name to this method of formation and its taste. *γλυκυς, sweet, κολλα, glue. Dessaignes* (1846) showed that glycocoll was formed as a decomposition product when hippuric acid was boiled with concentrated hydrochloric acid:



$$\begin{array}{l}COOH\\ |\\ CH_2NH{\cdot}COC_6H_5\end{array} + H_2O + HCl = \begin{array}{l}COOH\\ |\\ CH_2NH_2{\cdot}HCl\end{array} + C_6H_5COOH.$$

Hippuric acid benzoyl glycocoll. Glycocoll hydrochloride. Benzoic acid.

Strecker (1848) observed that glycocoll appeared from an analogous decomposition of the glycocholic acid occurring in bile (*cf.* Taurine, p. 376):



$$\begin{array}{l}COOH\\ |\\ CH_2NH_2{\cdot}C_{24}H_{39}O_4\end{array} + 2KOH = \begin{array}{l}COOK\\ |\\ CH_2NH_2\end{array} + C_{24}H_{39}O_5K + H_2O.$$

Glycocholic acid. Potassium amino-acetate. Potassium cholate.

Since then, glycocoll has been found to constitute a breakdown product of many other animal and vegetable proteins; it is especially abundant in the fibroin of silk.

Glycocoll was first (1858) prepared artificially by *Perkin* and *Duppa,* when they allowed ammonia to act on bromoacetic acid.

Properties.—Glycocoll crystallizes from water in large, rhombic prisms, which are soluble in 4 parts of cold water. By precipitation of its aqueous solution with absolute alcohol it is obtained as needles, chemically identical with the other form (Ber. **55,** 1066). It is insoluble in alcohol and ether. It possesses a sweetish taste, and melts with decomposition. Heated with barium hydroxide it breaks up into methylamine and carbon dioxide; nitrous acid converts it into glycollic acid. Ferric chloride imparts an intense red coloration to glycocoll solutions; acids discharge this, but ammonia restores it.

Metallic Salts.—An aqueous solution of glycocoll will dissolve many metallic oxides, forming salts. Of these, the *copper salt*, $(C_2H_4NO_2)_2Cu + H_2O$, is very characteristic, and crystallizes in dark blue needles: *silver salt*, $C_2H_4NO_2Ag$, crystallizes on standing over sulphuric acid. The combinations of glycocoll with salts, *e.g.* $C_2H_5NO_2{\cdot}KNO_3$, $C_2H_5NO_2{\cdot}AgNO_3$, are mostly crystalline.

Salts with acids.—Glycocoll yields the following compounds with hydrochloric acid: $C_2H_5NO_2{\cdot}HCl$ and $2(C_2H_5NO_2){\cdot}HCl$: the first is obtained with an excess of hydrochloric acid, and crystallizes in long prisms. *Nitrate*, $C_2H_5NO_2{\cdot}HNO_3$, forms large prisms.

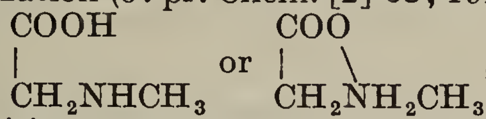
Ethyl aminoacetate, glycocoll ester, $NH_2{\cdot}CH_2COOC_2H_5$, b.p. 149°, b.p. 52°/10 mm., obtained from the hydrochloride with 33% NaO, is an oil resembling cocoa in odour, which is easily soluble in ether, alcohol, and water. In aqueous solution, however, it changes into diketopiperazine (p. 446), and in ether into triglycylglycine ester (p. 448). The ester is particularly suitable for the preparation of various derivatives of glycocoll (Ber. **34**, 436). *Glycocoll ester hydrochloride*, $HCl{\cdot}NH_2{\cdot}CH_2COOC_2H_5$, m.p. 144°, is formed by the passage of HCl gas into a mixture of alcohol and glycocoll, and can be employed as a method of estimation of glycocoll on account of its slight solubility in alcoholic hydrochloric acid (Ber. **39**, 548). It is also obtained from methyleneaminoacetonitrile (see below), aceturic acid (p. 442) (Ber. **29**, 760), or from the reaction product of hexamethyleneamine and potassium chloroacetate (C. 1899, I. 183, 420), by the action of alcoholic hydrochloric acid, whereby the ester hydrochloride results. This is also formed by pouring excess of alcohol on *glycyl chloride hydrochloride*, $HCl{\cdot}NH_2{\cdot}CH_2COCl$, which is prepared from precipitated glycocoll and phosphorus pentachloride in acetyl chloride, as a crystalline powder (Ber. **38**, 2914).

Glycocollamide, amino-acetamide, $NH_2CH_2CONH_2$, is produced when glycocoll is heated with alcoholic ammonia to 160°. It is a white mass which dissolves readily in water, and reacts strongly alkaline. The HCl-salt results on heating chloroacetic ester to 70° with alcoholic ammonia.

Glycocoll hydrazide, $NH_2CH_2CO{\cdot}NHNH_2$, m.p. 80–85°, is obtained from glycocoll ester and hydrazine hydrate, as a hygroscopic crystalline mass; *hydrochloride*, $C_2H_7N_3O{\cdot}2HCl$, m.p. 201° (J. pr. Chem. [2] **70**, 102).

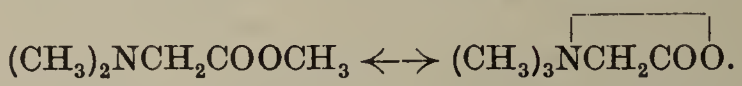
Glycocoll nitrile, amino-acetonitrile, NH_2CH_2CN, b.p. 58°/15 mm., is prepared from glycoll nitrile and alcoholic ammonia at 0°; *hydrochloride*, m.p. 165°; *sulphate*, $C_2H_4N_2{\cdot}H_2SO_4$, m.p. 101° (J. pr. Chem. [2] **65**, 189; Ber. **36**, 1511).

Methyleneaminoacetonitrile, $CH_2:NCH_2CN$, m.p. 129° (decomp.), is formed from formaldehyde, ammonium chloride, and potassium cyanide; also from glycocoll nitrile and formaldehyde. It may consist of a double molecule. It is remarkable for its ready crystallization (J. pr. Chem. [2] **65**, 192: Ber. **36**, 1506).

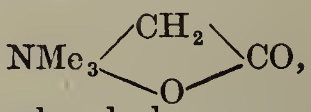
Methyl glycocoll, *sarcosine*,  $\begin{array}{l}COOH\\ |\\ CH_2NHCH_3\end{array}$ or $\begin{array}{l}COO\\ |\quad\backslash\\ CH_2NH_2CH_3\end{array}$, was first obtained by *Liebig* (1847) as a decomposition product of the creatine contained in beef extract. Its name is derived from σάρξ, flesh. *Volhard* (1862) prepared it synthetically by the action of methylamine on monochloroacetic acid; and it is also produced when creatine, $NH_2{\cdot}C(:NH){\cdot}NMe{\cdot}CH_2{\cdot}COOH$, or caffeine (p. 644) is heated with barium hydroxide solution. It dissolves readily in water but with difficulty in alcohol. The *nitrile* of sarcosine is obtained together with methylamine from methylene cyanohydrin, the additive product of formaldehyde and hydrocyanic acid (Ann. **279**, 39: J. pr. Chem. [2] **65**, 188).

It is readily soluble in water, but sparingly so in alcohol. It melts at 210–220° with decomposition into carbon dioxide and dimethylamine, yielding at the same time sarcosine anhydride (p. 447). It forms salts with acids, which show an acid reaction. Ignited with soda-lime it evolves methylamine. Sarcosine yields methylhydantoin with cyanogen chloride and creatine (*q.v.*) with cyanamide. *Sarcosine ethyl ester*, $CH_3NHCH_2CO_2C_2H_5$, b.p. 43°/10 mm. (Ber. **34**, 452).

Dimethyl glycocoll, $(CH_3)_2NCH_2COOH$, is prepared by the hydrolysis of its *nitrile, dimethylaminoacetonitrile*, $(CH_3)_2NCH_2CN$, b.p. 138°. This is formed by the action of dimethylamine on methyleneaminoacetonitrile (above) or on glycollic nitrile. *Dimethylaminoacetic methyl ester*, $(CH_3)_2NCH_2COOCH_3$, b.p. 135°, is obtained from the interaction of chloroacetic ester and dimethylamine. It is isomeric with betaine, into which it partly changes when heated. Betaine, when heated above its melting point (293°), forms an equilibrium mixture, in which the dimethylamino ester predominates (Ber. **35**, 584):



$$(CH_3)_2NCH_2COOCH_3 \longleftrightarrow (CH_3)_3NCH_2COO.$$

Betaine, *trimethylglycocoll*, *oxyneurine*,  $NMe_3{<}\overset{CH_2}{\underset{O}{}}{>}CO$, or better, $NMe_3{}^{+}{\cdot}CH_2{\cdot}COO^{-}$ (Pfeiffer, Ber. **55**, 1762), has already been mentioned (p. 379) in connection with choline, from which it is prepared by oxidation.

Its *hydrochloride* is prepared by the union of monochloroacetic acid with trimethylamine (Ber. **2**, 167 : **3**, 161 : **35**, 603):

$$ClCH_2COOH + N(CH_3)_3 = ClN(CH_3)_3CH_2COOH.$$

Similarly, chloroacetic ester and trimethylamine yield *betaine ester hydrochloride*, $ClN(CH_3)_3CH_2{\cdot}CO_2C_2H_5$, m.p. 143° (Ber. **38**, 167). Betaine is also obtained by the methylation of glycocoll by means of methyl iodide, potassium hydroxide, and methyl alcohol. It occurs in beet-root (*Beta vulgaris*) (*Scheibler*, Ber. **2**, 292 : **3**, 155), and is to be extracted from beet molasses, in which it is the substance which gives rise to the trimethylamine obtained therefrom (p. 197). It also occurs in the leaves and stalks of *Lycium barbarum*, in cotton seeds, and in germ of malt and wheat (Ber. **26**, 2151).

It crystallizes in deliquescent crystals in which the acid, $HON(CH_3)_3CH_2COOH$, may be present. At 100° this ammonium hydroxide derivative loses one molecule of water, forming a *cyclic ammonium salt*, $ON(CH_3)_3CH_2CO$, which melts at 293°, with partial conversion into dimethylaminoacetic methyl ester (see above). Iodine in potassium iodide precipitates a *periodide* from an aqueous solution of betaine (C. 1904, II. 950).

Ethylamino derivatives. The action of ethylamine, diethylamine and triethylamine on chloroacetic acid produces *ethylglycocoll*, *diethylglycocoll*, and *triethylglycocoll*, *triethylbetaine*, $(C_2H_5)_3NCH_2COO$. Similarly to betaine itself, the latter compound is converted by destructive distillation into *diethylaminoacetic ethyl ester*, b.p. 177°, the ethiodide of which is reconverted by silver oxide into triethyl betaine. Similar changes have been observed with dimethylethyl betaine and methyldiethylbetaine (Ber. **35**, 584).

The **homologous betaines** can also be prepared by the addition of iodoalkyls to dialkylaminoacetonitriles and the subsequent saponification of the iodo-alkylate formed. The *dialkylaminoacetonitriles* just referred to can be synthesized from formaldehyde, hydrocyanic acid, and dialkylamines (Ber. **36**, 4188).

$$(C_2H_5)_2NCH_2CN \xrightarrow{CH_3I} (C_2H_5)_2N(CH_3I)CH_2CN \longrightarrow (C_2H_5)_2N(CH_3)CH_2COO.$$

Acyl Derivatives. *Formylglycocoll*, *formaminoacetic acid*, $HCONH{\cdot}CH_2{-}COOH$, m.p. 151–152°, is prepared by heating glycocoll with formic acid to 100°; and from glyoxylic acid and ammonia (Ber. **36**, 2525 : **38**, 3999).

$$\underset{\text{Glyoxylic acid.}}{2CHO{\cdot}COOH} + NH_3 = \underset{\text{Formyl glycine.}}{HCO{\cdot}NH{\cdot}CH_2COOH} + CO_2 + H_2O.$$

Acetylglycocoll, *acetaminoacetic acid*, *aceturic acid*, $CH_3CONH{\cdot}CH_2COOH$, m.p. 206°, results from the action of acetyl chloride on silver glycocoll; from acetamide and monochloroacetic acid; from ammonia and a mixture of glyoxylic and pyroracemic acids (Ber. **36**, 2526). It is readily soluble in water and alcohol, and behaves as a monobasic acid (Ber. **17**, 1664).

More important are *hippuric acid* or benzoyl glycocoll (*q.v.*) and glycocholic acid (*q.v.*) which have already been referred to in connection with glycocoll, and which will be dealt with later. They are similarly constituted to aceturic acid. *Naphthalenesulphoglycine*, $C_{10}H_7SO_2NH{\cdot}CH_2COOH$, m.p. 156° (Ber. **35**, 3779).

Di- and tri-glycollamic acids are formed on boiling monochloroacetic acid with concentrated aqueous ammonia (Ann. **122**, 269 : **145**, 49 : **149**, 88).

Diglycollamic acid, $NH(CH_2CO_2H)_2$, m.p. 225°, forms salts both with acids and bases, whilst *triglycollamic acid*, $N(CH_2CO_2H)_3$, cannot unite with acids.

Imino-acetonitrile, $NH(CH_2CN)_2$, m.p. 75°, and *triglycollamic nitrile*, $N(CH_2CN)_3$, m.p. 126°, are obtained from methylene cyanohydrin and ammonia (Ann. **278**, 229 : **279**, 39). *Dimethyl-dicyano-methyl-ammonium bromide*, $(CH_3)_2NBr(CH_2CN)_2$, is prepared from dimethylaminoacetonitrile and bromoacetonitrile (Ber. **41**, 2123).

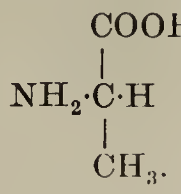
Alanine, *α-aminopropionic acid*, $CH_3\overset{*}{C}H(NH_2)CO_2H$ (see also below), m.p. 293° (decomp.), is obtained from α-chloro- and α-bromopropionic acid by means of ammonia ; also from aldehyde-ammonia, hydrocyanic acid, and hydrochloric acid ; or aldehyde, ammonium cyanide, and hydrochloric acid (Ber. **41**, 2061), by hydrolysis of the intermediate *α-amino-propionitrile*, $CH_3CH(NH_2)CN$. This can be precipitated as sulphate from an alcoholic solution of aldehyde-ammonia and hydrocyanic acid by sulphuric acid, and may be resolved into its optically active components by formation of the tartrates (p. 72) (C. 1904, I. 360).

It can be prepared by the action of hydrogen and ammonia on pyruvic acid in the presence of colloidal palladium (Compt. rend. **186**, 1844).

Racemic or *dl*-alanine crystallizes from water in aggregates of hard needles ; it is soluble in 3 parts of water, less easily in alcohol, and not at all in ether. On being quickly heated, it melts with partial decomposition, partially into ethylamine and CO_2, and partially into aldehyde, CO, and ammonia (Ber. **25**, 3502 : **32**, 245). Alanine is partially oxidized to pyruvic acid when shaken with air in the presence of copper (Compt. rend. **176**, 1227).

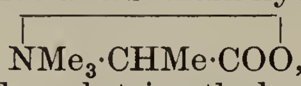
Amide, $CH_3{\cdot}CH(NH_2){\cdot}CONH_2$, m.p. 68° (C. 1906, I. 818). *Alanine ethyl ester*, $CH_3CH(NH_2)COOC_2H_5$, b.p. 48°/11 mm. ; *hydrochloride* is easily soluble in alcohol, unlike glycine ester hydrochloride (Ber. **34**, 442). *Alanyl chloride hydrochloride*, $CH_3CH(NH_3Cl)COCl$, is a white crystalline powder (Ber. **38**, 2917). *β-Naphthalenesulpho-alanine*, $C_{10}H_7SO_2{\cdot}NHCH(CH_3)COOH$, m.p. 152°. *Benzoylalanine*, $C_6H_5CO{\cdot}NHCH(CH_3)COOH$, m.p. 165°, is resolved by means of brucine into the components *d*- and *l*-benzoylalanines, which, on hydrolysis, yield *l*- and *d*-alanine.

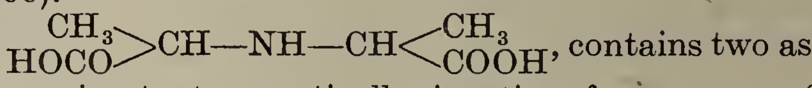
Dextrorotatory alanine, dec. 297°, $[\alpha]_D^{20}$ $+2{\cdot}7°$ (in water), $[\alpha]_D^{20}$ $+10{\cdot}4°$ in hydrochloric acid (Ber. **39**, 462 : **40**, 3721), occurs among the products of hydrolysis of many proteins, and can be isolated as ester in large amount from the hydrolysis products of silk fibroin. It forms rhombic crystals. The naturally occurring alanine has been shown (*Freudenberg* and *Rhino*, Ber. **57**, 1550) to belong to the same stereochemical series as *l*-(+)-lactic acid, and is therefore to be designated *l*-alanine, in spite of its dextrorotation. Its formula can be written accordingly :



$$\begin{array}{c} COOH \\ | \\ NH_2{\cdot}C{\cdot}H \\ | \\ CH_3. \end{array}$$

Nitrous acid converts *l*-(+)-alanine into ordinary *l*-(+)-lactic acid. Nitrosyl bromide, on the other hand, converts *l*-(+)-alanine into (−)-bromopropionic acid, which with ammonia yields *d*-(−)-alanine, and similarly *d*-(−)-alanine with nitrosyl bromide followed by ammonia yields *l*-(+)-alanine (Walden inversion) (Ber. **58**, 148). For the relationship of alanine to serine and cystine, see Ber. **40**, 3717.

Methyl iodide and sodium hydroxide convert *l*-(+)-alanine into (−)-*trimethylpropiobetaine*,  $\overbrace{\mathrm{NMe_3{\cdot}CHMe{\cdot}COO}}$, which is also obtained from (+)-α-bromopropionic acid and trimethylamine (Ber. **40**, 5000). *Triethylpropiobetaine* is formed by the hydrolysis of the ethiodide of α-*diethylaminopropionitrile*, $CH_3{\cdot}CH(NEt_2){\cdot}CN$, b.p. 81°/27 mm., which is obtained from aldehyde cyanohydrin and diethylamine (Ber. **36**, 4188).

Iminodipropionic acid,  $\mathrm{{}^{CH_3}_{HOCO}\!>\!CH{-}NH{-}CH\!<\!{}^{CH_3}_{COOH}}$, contains two asymmetric carbon atoms, giving rise to two optically inactive forms, m.p. 255° (corresponding with mesotartaric acid), and m.p. 235° (corresponding with racemic acid). The *monamides*, m.pp. 332° and 210°, are formed by the prolonged interaction of dilute hydrocyanic acid and aldehyde-ammonia at ordinary temperatures, together with *iminodipropionimide*, $NH[CH(CH_3)CO]_2NH$, m.p. 186°, alanine, and other substances (Ber. **39**, 3942).

Higher α-amino-acids are prepared mainly by the general methods from α-halogen-fatty acids and from the nitriles of α-hydroxy-acids and ammonia.

α-Amino-*n*-butyric acid, $CH_3CN_2\overset{*}{C}H(NH_2)COOH$, m.p. 307° (decomp.), is resolved by means of the morphine salt of the benzoyl-derivative. $[\alpha]_D^{20} \pm 8°$; *ethyl ester*, b.p. 61°/11 mm. (Ber. **33**, 2387 : **34**, 443) ; *nitrile* (Ber. **41**, 2062). α-*Amino*-iso*butyric acid*, $(CH_3)_2C(NH_2)CO_2H$, sublimes at 280° without melting, and is formed also by oxidation of diacetonamine sulphate ; *nitrile*, b.p. 50°/12 mm., is prepared from acetone and ammonium cyanide (Ber. **33**, 1900 : **39**, 1181 1726).

α-Amino-valeric acid, $CH_3[CH_2]_2CH(NH_2)COOH$, is formed also by oxidation of benzoyl coniine (Ber. **19**, 500) ; *ethyl ester*, b.p. 68°/8 mm. (Ber. **35**, 1004).

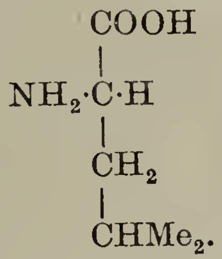
Valine, α-*Amino*-iso*valeric acid*, $(CH_3)_2CH\overset{*}{C}H(NH_2)COOH$, decomposes at 298°. The inactive acid results from α-bromo*iso*valeric acid and ammonia ; *ethyl ester*, b.p. 63°/8 mm. *Formyl valine*, $HCONHCH(C_3H_7)COOH$, m.p. 140–145°, is produced by heating valine and formic acid together. Formylvaline can be resolved by means of its brucine salts, and the active valines obtained from the active formyl derivatives. The dextrorotatory valine, m.p. 315°, $[\alpha]_D^{20} = +6{\cdot}42°$, in aqueous solution and $+28{\cdot}8°$ in hydrochloric acid, is a decomposition product of protein bodies—in the germs of the lupin, horn, casein, from protamines, and from the pancreas of oxen. (−)-Valine has a much sweeter taste than (+)-valine (Ber. **39**, 2320). α-*Aminomethylethylacetic acid*, $(C_2H_5)(CH_3)C(NH_2)COOH$, is prepared from methyl ethyl ketone, etc. ; *ethyl ester*, b.p. 66°/20 mm. (Ber. **35**, 400 : **39**, 1189).

α-Aminocaproic acids, α-*amino*-n-*caproic acid*, $CH_3[CH_2]_3\overset{*}{C}H(NH_2)COOH$, s prepared from α-bromo-*n*-caproic acid and ammonia. It is resolved into its optical components by means of its benzoyl-derivative (Ber. **33**, 2381 : **34**, 3764).

Leucine, α-*Amino*-iso*caproic acid*, $(CH_3)_2CHCH_2\overset{*}{C}H(NH_2)COOH$. Optically active leucine (from λευκός, glistening white, referring to the appearance of the scaly crystals) occurs in different animal fluids, in the pancreas, in the spleen, in the lymph-glands, and is physiologically very important. It is formed by the decay of proteins, or when they are boiled with alkalis and acids. It is prepared by heating horn, the dried cervical ligament of oxen, or from casein with dilute sulphuric acid. Its purification is best effected by conversion into the ester (Ber. **34**, 446 : C. 1908, I. 1633). Leucine is also obtained from vegetable proteins such as that of the lupin. *Strecker* (1848) showed that when it was treated with nitrous acid it passed into a hydroxycaproic acid, *leucic acid*, m.p. 73° (p. 418).

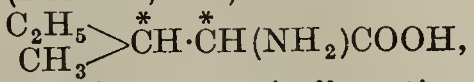
The naturally occurring leucine, m.p. 270°, sublimes unaltered when carefully heated, but decomposes on rapid rise of temperature into amylamine and CO_2. It forms shining leaflets, which feel greasy to the touch. It is soluble in 48 parts of water and 800 parts of hot alcohol. It is optically active, the *free acid* rotating the plane of polarization to the *left*, whilst its *hydrochloride* rotates it to the *right*. When heated with alkalis it becomes inactive and is then identical with the synthetic product, which can be obtained from *iso*valeraldehyde, ammonium cyanide and hydrochloric acid, or from the condensation product of *iso*butyraldehyde and hippuric acid.

The active leucines can be obtained by resolution of *dl*-benzoylleucine by means of cinchonine, or by resolution of *dl*-formylleucine. (+)-Leucine is obtained from inactive leucine by the action of *Penicillium glaucum*, its hydrochloride is lævorotatory (Ber. **24**, 669 : **26**, 56 : **33**, 2370). As all naturally occurring amino-acids probably belong to the same stereochemical series, the natural (−)-leucine is probably *l*-leucine, and can be represented



$$\begin{array}{c} COOH \\ | \\ NH_2{\cdot}C{\cdot}H \\ | \\ CH_2 \\ | \\ CHMe_2. \end{array}$$

Leucine ethyl ester, b.p. 196°. *Acetyl leucine*, m.p. 160° (Ber. **34**, 433). *Leucyl chloride hydrochloride*, $C_4H_9CH(NH_3Cl)COCl$ (Ber. **38**, 615).

α-Amino-*sec.*-butylacetic acid, iso*leucine*,  $\genfrac{}{}{0pt}{}{C_2H_5}{CH_3}{>}\overset{*}{C}H{\cdot}\overset{*}{C}H(NH_2)COOH$, contains 2 asymmetric carbon atoms, and therefore gives rise to 4 optically active components and 2 racemic forms. *Resolution*, see Z. physiol. Chem. 1931, **195**, 121. A *d*-iso*leucine*, m.p. 280°, with decomposition, $[\alpha]_D^{20} = +9{\cdot}7$ in water, $+36{\cdot}8$ in hydrochloric acid, occurs together with leucine in beet molasses, and as a decomposition product of proteins. Synthetically, *rac.-iso*leucine is produced by reduction of α-oximino-*iso*butylacetic acid (p. 465), and from α-bromo-*sec.*-butylacetic acid and ammonia. *d-iso*Leucine is prepared from *d*-valeric aldehyde by the cyanohydrin synthesis (Ber. **40**, 2538 : **41**, 1453).

α-*Amino-œnanthic acid*, $CH_3[CH_2]_4CH(NH_2)CO_2H$ (Ber. **8**, 1168).

α-*Amino caprylic acid*, $CH_3[CH_2]_5CH(NH_2)CO_2H$ (Ann. **176**, 344).

α-*Aminopalmitic acid*, $CH_3[CH_2]_{13}CH(NH_2)CO_2H$ (Ber. **24**, 941).

α-*Aminostearic acid*, $CH_3[CH_2]_{15}CH(NH_2){\cdot}CO_2H$, m.p. 221° (Ber. **24**, 2395).

Dipeptides and Polypeptides

As has repeatedly been mentioned, the simple α-amino-acids, such as glycocoll, alanine, valine, and leucine, occur together, and also with such complicated substances as serine, proline, cystine, asparagine, lysine, arginine, histidine, and tyrosine, as products of the hydrolytic decomposition of proteins. It is probable that these breakdown bodies are united with one another in the protein molecule through their amide groups.

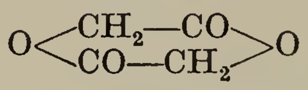
This question has been attacked both synthetically and analytically (*E. Fischer :* Untersuchungen über Amino-säuren, Polypeptide und Proteine, Berlin, 1906 : *Th. Curtius :* Verkettung von Amino-säuren J. pr. Chem. [2] **70**, 57). In synthesis, the esters, chlorides, and azides of the aminocarboxylic acids themselves or of the substances which go to produce them, have been employed; and by their means the aminoacyl residue has been substituted into the amino-group of other amino-acids, and the process has been successively repeated. The aminoacyl aminocarboxylic acids produced have been named by E. Fischer, *peptides*, because of their comparability with the natural *peptones* (protein products of digestion). They are classified according to the number of the connected amino-acids—*di-*, *tri-*, *tetra-peptides*, etc.

In recent years it has been questioned, whether the peptide linkage is the only one occurring in the protein molecule, or whether closed heterocyclic rings may not also play a part. This is discussed further under the proteins.

1. **Dipeptides** and their **inner anhydrides,** *cyclic double amides, diketopiperazines.* α-Amino-esters, when heated or even on standing in aqueous solution, part with alcohol and form dimolecular cyclic amides, corresponding with the lactides (p. 414):

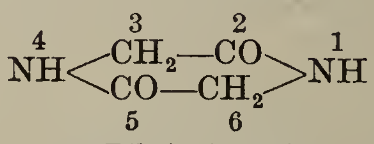
$$2NH_2CH_2COOC_2H_5 = NH{<}\begin{smallmatrix}CH_2-CO\\CO-CH_2\end{smallmatrix}{>}NH + 2C_2H_5OH.$$

These compounds are derivatives of diethylenediamine or piperazine (p. 387), whence the names diketo-, diaci-, or dioxopiperazine:



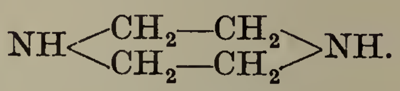
$$O{<}\begin{smallmatrix}CH_2-CO\\CO-CH_2\end{smallmatrix}{>}O$$

Diglycollide.



$$\overset{4}{NH}{<}\begin{smallmatrix}\overset{3}{CH_2}-\overset{2}{CO}\\\underset{5}{CO}-\underset{6}{CH_2}\end{smallmatrix}{>}\overset{1}{NH}$$

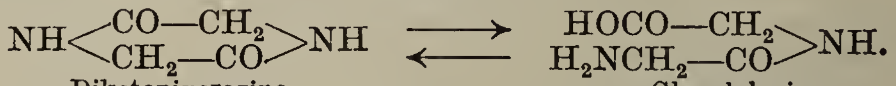
2 : 5-Diketopiperazine.



$$NH{<}\begin{smallmatrix}CH_2-CH_2\\CH_2-CH_2\end{smallmatrix}{>}NH.$$

Piperazine.

When warmed for a short time with hydrochloric or hydrobromic acid, or when shaken with dilute alkalis, the diketopiperazine is split up into the dipeptide, which when melted, or when its ester is heated, easily changes into the diketopiperazine:



$$NH{<}\begin{smallmatrix}CO-CH_2\\CH_2-CO\end{smallmatrix}{>}NH \rightleftarrows \begin{smallmatrix}HOCO-CH_2\\H_2NCH_2-CO\end{smallmatrix}{>}NH.$$

Diketopiperazine. Glycylglycine (the simplest dipeptide).

Unsymmetrically substituted diketopiperazines, such as leucylglycine anhydride, can be split into two different dipeptides, from which the same anhydride can be re-formed.

2. **Dipeptides** and **polypeptides** are obtained in the following manner: (*a*) Chlorides of the α-halogen-fatty acids react with α-amino-acids to form α-halogenacylamino-acids, which with ammonia give dipeptides. These by further treatment with α-halogen acyl chlorides and ammonia yield tripeptides, and these tetrapeptides, pentapeptides, and so on:

$$\underset{\text{Chloroacetylglycine.}}{ClCH_2CO{\cdot}NHCH_2COOH} \xrightarrow{NH_3} \underset{\text{Glycylglycine.}}{NH_2CH_2CO{\cdot}NHCH_2COOH} \longrightarrow$$

$$\underset{\text{Chloroacetylglycylglycine.}}{ClCH_2CO{\cdot}NHCH_2CO{\cdot}NHCH_2COOH} \xrightarrow{NH_3}$$

$$\underset{\text{Diglycylglycine.}}{NH_2CH_2CO{\cdot}NHCH_2{\cdot}CO{\cdot}NHCH_2COOH.}$$

The esters of the halogenacylamino-acids are easily converted by ammonia into dipeptide anhydrides, diketopiperazines (see above).

(*b*) Again, the halogenacylamino-acids can be converted into their chlorides, united with other amino-acids and then be acted on by ammonia:

$$\underset{\text{Bromo}\textit{iso}\text{caproylglycyl chloride.}}{C_4H_9CHBrCO{\cdot}NHCH_2COCl} \longrightarrow$$

$$\underset{\text{Bromo}\textit{iso}\text{caproylglycylglycine.}}{C_4H_9CHBrCO{\cdot}NHCH_2CO{\cdot}NHCH_2COOH} \xrightarrow{NH_3}$$

$$\underset{\text{Leucylglycylglycine.}}{C_4H_9CH(NH_2)CO{\cdot}NHCH_2COOH.}$$

(*c*) Finally, the chlorides of the amino-carboxylic acid hydrochlorides can be employed with advantage (p. 436). The azides, also, of the acyl amino-acids such as hippuryl azide, $C_6H_5\cdot CONHCH_2CON_3$, unite with amino-acids, splitting off N_3H, and easily forming acyl derivatives of the di- and polypeptides.

3. Higher polypeptides result from heating the methyl esters of lower peptides :

$$\underset{\text{Diglycylglycine ester.}}{2NH_2CH_2CO\cdot NHCH_2CO\cdot NHCH_2CO_2CH_3} \longrightarrow \underset{\text{Pentaglycylglycine ester.}}{NH_2CH_2CO\cdot [NHCH_2CO]_4NHCH_2CO_2CH_3}.$$

4. Some di- and polypeptides are produced by the partial hydrolysis of various proteins, such as silk fibroin, elastin, gliadin, gelatin with cold fuming hydrochloric acid or by enzymic digestion. By the use of uniform enzyme preparations under optimal conditions and hydrolysis to a definite stage, this fractional enzymic hydrolysis is of great value (*Waldschmidt-Leitz*, Z. physiol. Chem. **156**, 68, 99).

Properties.—The di- and polypeptides are usually soluble in water, though some, such as the penta- and hexapeptides from glycine are only sparingly so. They are soluble in acids and alkalis, in accord with their content of an amino and a carboxyl group. Most peptides are insoluble in alcohol. The peptides decompose, with or without melting, at about 200°, the dipeptides usually forming diketopiperazines.

The higher peptides, such as Curtius's " *biuret base* " (Triglycylglycine ester), give the biuret reaction, which is characteristic of proteins, when treated with alkali and copper sulphate (see under Proteins).

Di- and polypeptides are broken down to their constituent amino-acids by the erepsin of pancreatic juice and intestinal mucosa (Z. physiol. Chem. **151**, 31). Hydrochloric acid also hydrolyses them to amino-acids.

Glycylglycine, $NH_2CH_2CO\cdot NHCH_2COOH$, decomposes 215–220° ; *ethyl ester*, m.p. 89°, easily parts with alcohol, yielding **glycine anhydride,** 2 : 5-*diketopiperazine*, $\overline{NHCH_2CO\cdot NHCH_2CO}$, m.p. 275°, which is also prepared from glycocoll ester in aqueous solution. By boiling for a short time with strong hydrochloric acid or by shaking with N/1 sodium hydroxide, it is easily split up into glycylglycine (Ber. **38**, 607).

Sarcosine anhydride, $CH_3\overline{NCH_2CON(CH_3)CH_2CO}$, m.p. 150°, b.p. 350°, is obtained by heating sarcosine (Ber. **17**, 286) : molecular compounds with phenols, Z. angew. Chem. **40**, 983.

Glycyl-dl-*alanine*, $NH_2CH_2CO\cdot NHCH(CH_3)COOH$, m.p. 227° (decomp.), is prepared from chloroacetylalanine and ammonia ; *anhydride*, m.p. 245° with decomposition, is formed from chloroacetylalanine ester and ammonia.

Glycyl-l-(+)-alanine and its *anhydride* are obtained by the hydrolysis of silk fibroin (Ber. **40**, 3546). *l-(+)-Alanylglycine*, $CH_3CH(NH_2)CO\cdot NHCH_2COOH$, m.p. 235° with decomposition, is produced from *l*-(+)-alanyl chloride hydrochloride and glycocoll ester (Ber. **38**, 2914).

Alanylalanine, $CH_3CH(NH_2)CO\cdot NHCH(CH_3)COOH$, m.p. 276° (decomp.), is obtained by the decomposition by alkali of its anhydride, *di-lactyl di-amide*, *lactimide*, dimethyldiketopiperazine, $NH{<}\genfrac{}{}{0pt}{}{CH(CH_3)CO}{CO\cdot CH(CH_3)}{>}NH$, m.p. 275°. The anhydride is best obtained from alanine ester at 180°. It is reduced by sodium and alcohol to 2 : 5-dimethylpiperazine (Ber. **38**, 2376 : C. 1902, I. 631). *d*-(−)-*Alanyl l-(+)-alanine* is produced from *l*-bromopropionyl *l*-(+)-alanine and ammonia, $[\alpha]_D^{20} = -68{\cdot}5°$; its ester on parting with alcohol is converted into the optically inactive meso-anhydride (see p. 41).

α-Aminobutyryl α-aminobutyric acid, $NH_2CH(C_3H_7)CO{\cdot}NHCH(C_3H_7)COOH$, 2 stereoisomeric forms, m.p. 273° (decomp.), and m.p. 257° (decomp.) is prepared from bromobutyrylaminobutyric acid; *anhydride*, m.p. 267° (Ann. **340**, 187).

Leucylleucine, $NH_2CH(C_4H_9)CONHCH(C_4H_9)COOH$, m.p. 270° with decomposition, is formed from bromo*iso*caproyl leucine and ammonia; *anhydride leucinimide*, m.p. 271°, is prepared from leucine ester (Ber. **37**, 2491).

Diglycylglycine, $NH_2CH_2CO{\cdot}NHCH_2CO{\cdot}NHCH_2COOH$, m.p. 246° (decomp.), is prepared from chloroacetylglycylglycine and ammonia; *methyl ester*, m.p. 111°, when heated passes into *pentaglycylglycine ester*, slightly soluble in water (Ber. **39**, 472).

Triglycylglycine is prepared from chloroacetyldiglycylglycine; *ester*, $NH_2CH_2CO{\cdot}NHCH_2CO{\cdot}NHCH_2CO{\cdot}NHCH_2COOC_2H_5$, the "*biuret base*," is formed together with a little glycine anhydride, when glycocoll is left to stand in solution in absolute ether. *Benzoyl triglycyl glycine*, m.p. 217°, is formed also from hippuryl glycine azide and glycyl glycine (Ber. **37**, 1284, 2486).

Leucylpentaglycylglycine, $C_4H_9CH(NH_2)CO[NHCH_2CO]_5NHCH_2COOH$, is prepared from bromo*iso*caproylpentaglycylglycine and ammonia (Ber. **39**, 461).

The most complex polypeptide synthesized is l-*leucyltriglycyl*-l-*leucyltriglycyl* l-*leucyltriglycyl*-l-*leucylpentaglycylglycine* (Ber. **49**, 561).

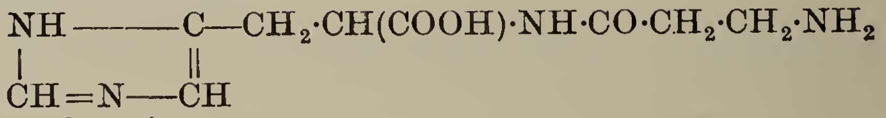
β-Amino-acids

In addition to the methods 1 to 4 on p. 434, β-amino acids are advantageously prepared by the addition of hydroxylamine to αβ-unsaturated acids. The probable intermediate product, a hydroxylamino-acid is reduced to the amino-acid by excess of hydroxylamine (Ann. **389**, 1). β-Imino acids can also be reduced catalytically to β-amino acids.

Of this group of substances little is known. They form neither cyclic double amides, as do the α-amino-acids, nor cyclic simple amides or lactams like the higher amino-acids, except betaines.

β-Aminopropionic acid, β-alanine, $CH_2(NH_2)CH_2{\cdot}COOH$, m.p. 196° with decomposition into ammonia and acrylic acid. It is isomeric with alanine (p. 443), and is prepared from β-iodopropionic acid and ammonia, from β-nitropropionic acid, from *iso*serine (α-hydroxy-β-aminopropionic acid) by reduction with hydriodic acid and phosphorus (Ber. **35**, 3796); but most conveniently from succinimide, by the Hofmann inversion (p. 191) by means of bromine and alkali (Ber. **26**, R. 96: C. 1905, I. 155: 1906, I. 818); *methyl ester*, b.p. 58°/15 mm.; *amide*, m.p. 40°.

β-Aminopropionic acid forms with histidine the dipeptide *carnosine*, which occurs in muscle extract.



$$\begin{matrix} NH & \text{———} & C\text{—}CH_2{\cdot}CH(COOH){\cdot}NH{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2 \\ | & & \| \\ CH{=}N & \text{——} & CH \end{matrix}$$

Carnosine.

β-Dimethylaminopropionic methyl ester, $(CH_3)_2NCH_2CH_2COOCH_3$, b.p. 154°, is prepared from β-iodopropionic ester and dimethylamine. Heat partially transforms it into its isomer *β-trimethylpropiobetaine*, $(CH_3)_3NCH_2CH_2COO$, which in its turn undergoes transformation on melting into trimethylamine acrylate, $CH_2:CHCOONH(CH_3)_3$ (Ber. **35**, 584).

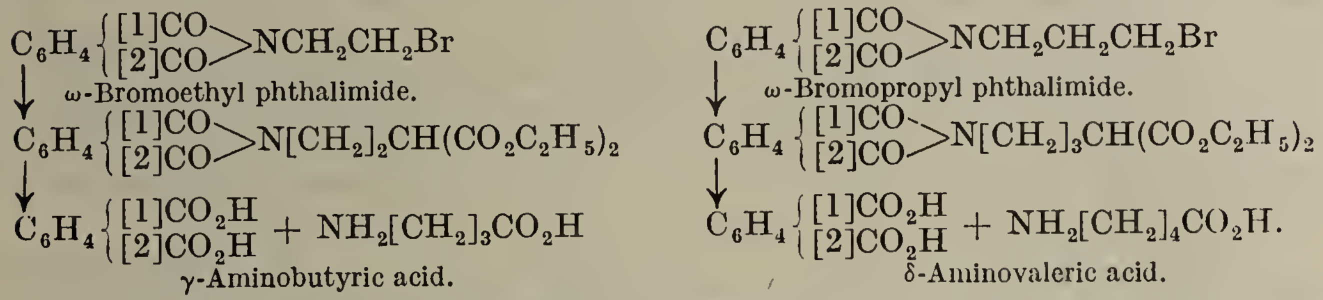
β-Aminobutyric acid, $CH_3CH(NH_2)CH_2CO_2H$, m.p. 156° (approx.), is prepared by heating crotonic acid with ammonia. It is a very hygroscopic crystalline mass (J. pr. Chem. [2] **70**, 204). *β-Amino*iso*valeric acid*, $(CH_3)_2C(NH_2)CH_2{\cdot}COOH$, is produced by the reduction of the corresponding nitro-acid (p. 434).

γ-, δ-, ε-, and ζ-Aminocarboxylic Acids

The most important characteristic of the γ- and δ-amino-carboxylic acids as well as of some of the higher acids is that when heated they part with water and yield cyclic, simple acid amides or lactams (p. 450).

(1) Piperidine derivatives, when oxidized, have yielded some of these acids (*Schotten*). (2) Potassium phthalimide affords a general synthetic method: ethylene bromide or trimethylene bromide, acted on by it, yields ω-bromoethyl

phthalimide and ω-bromopropyl phthalimide (*Gabriel*). These compounds react with the sodium derivatives of malonic or alkylmalonic esters, or cyanoacetic esters to form phthalimido-acids which are decomposed on heating with hydrochloric acid, into phthalic acid, γ-, or δ-amino-carboxylic hydrochloride, carbon dioxide and alcohol (Ber. **24**, 2450):



$$C_6H_4\left\{\begin{matrix}[1]CO\\ [2]CO\end{matrix}\right.\!>NCH_2CH_2Br \qquad C_6H_4\left\{\begin{matrix}[1]CO\\ [2]CO\end{matrix}\right.\!>NCH_2CH_2CH_2Br$$

ω-Bromoethyl phthalimide. ω-Bromopropyl phthalimide.

$$\downarrow \qquad\qquad \downarrow$$

$$C_6H_4\left\{\begin{matrix}[1]CO\\ [2]CO\end{matrix}\right.\!>N[CH_2]_2CH(CO_2C_2H_5)_2 \qquad C_6H_4\left\{\begin{matrix}[1]CO\\ [2]CO\end{matrix}\right.\!>N[CH_2]_3CH(CO_2C_2H_5)_2$$

$$\downarrow \qquad\qquad \downarrow$$

$$C_6H_4\left\{\begin{matrix}[1]CO_2H\\ [2]CO_2H\end{matrix}\right. + NH_2[CH_2]_3CO_2H \qquad C_6H_4\left\{\begin{matrix}[1]CO_2H\\ [2]CO_2H\end{matrix}\right. + NH_2[CH_2]_4CO_2H.$$

γ-Aminobutyric acid. δ-Aminovaleric acid.

Similarly, ε-bromo-amyl phthalimide can be made to yield ε-phthalimido-amyl malonic ester, and this converted into ζ-aminoheptylic acid (Ber. **35**, 1367). Or, benzoyl amino-amyl iodide may easily be made to react with potassium cyanide or sodium malonic ester, the product from which is hydrolysed.

(3) A general method for the preparation of δ-, ε-, and ζ-amino-acids and their lactams, is the transformation of the oximes of cyclic ketones, such as *cyclo*pentanone, *cyclo*hexanone or *cyclo*heptanone (Vol. II). These are converted by concentrated sulphuric acid into lactams (*cf. Beckmann's transformation*, p. 268) which can be decomposed into their respective amino-acids (*Wallach*, Ann. **312**, 171), *e.g.*:

*cyclo*Pentanone oxime. δ-Aminovaleric acid lactam.

Mechanism of these transformations and the Beckmann inversion generally, see Ann. **346**, 27.

γ-Aminobutyric acid, *piperidic acid*, m.p. 183–184°. It is formed (1) when piperidyl urethane, $CH_2{<}^{CH_2CH_2}_{CH_2CH_2}{>}N\cdot CO_2C_2H_5$, is oxidized with nitric acid (Ber. **16**, 644); (2) by means of potassium phthalimide; (*a*) by the double decomposition of bromoethylphthalimide with sodium malonic ester (see above), or (*b*) from ω-bromopropylphthalimide and potassium cyanide, and decomposing the phthalyl γ-aminobutyric nitrile (Ber. **23**, 1772). The acid is most conveniently obtained from its lactam (p. 450) by means of barium hydroxide solution (Ber. **33**, 2230). *γ-Dimethylaminobutyric methyl ester*, $(CH_3)_2N[CH_2]_3COOCH_3$, b.p. 172°, is prepared from γ-chlorobutyric ester and dimethylamine. On heating it is decomposed into butyrolactone and trimethylamine. The isomeric *γ-trimethylbutyrobetaine*, $(CH_3)_3N[CH_2]_3COO$, which is obtained by exhaustive methylation of butyrolactam in alkaline solution (Ber. **35**, 617) undergoes the same decomposition.

γ-Aminovaleric acid, $CH_3CH(NH_2)CH_2CH_2CO_2H$, m.p. 193°, results from the decomposition of lævulinic acid phenylhydrazone by sodium amalgam (Ber. **27**, 2313). Both γ-amino-acids, when heated, pass into lactams.

δ-Amino-*n*-valeric acid, *homopiperidic acid*, $NH_2(CH_2)_4CO_2H$, m.p. 158°, is produced by the putrescence of fibrin, flesh, and gelatin (Ber. **31**, 776). The benzoyl derivative of this acid and also *sulphonyl bis-δ-aminovaleric acid*, $SO_2[NH(CH_2)_4CO_2H]_2$, m.p. 163°, are formed by the oxidation of benzoylpiperidine, $C_5H_{10}N\cdot COC_6H_5$, and of sulphopiperidine by $KMnO_4$ (Ber. **21**, 2240); the acid is prepared from phthalimido-propylmalonic ester (Ber. **23**, 1769).

δ-Trimethylvalerobetaine, $(CH_3)_3N[CH_2]_4COO$. The *hydrobromide* is obtained from γ-bromopropylmalonic esters and trimethylamine, by hydrolysis, and the action of hydrobromic acid. The substance itself is converted by heat into the isomeric *δ-dimethylaminovaleric methyl ester*, $(CH_3)_2N[CH_2]_4COOCH_3$, b.p. 186–189°, together with δ-valerolactone (Ber. **37**, 1853).

By method 2 (p. 448) the following are also prepared: *δ-amino-α-methylvaleric acid*, $NH_2\cdot CH_2CH_2CH_2CH(CH_3)CO_2H$, m.p. 168°; *δ-amino-α-ethylvaleric acid*, $NH_2CH_2CH_2CH_2CH(C_2H_5)CO_2H$, m.p. 200–200·5°; *δ-Amino-α-propyl-*

valeric acid, $NH_2CH_2CH_2CH_2CH(C_3H_7)CO_2H$, m.p. 186° (Ber. **24**, 2444). A *β*- or *γ*-methyl δ-amino-*n*-valeric acid, m.p. 134°, with decomposition, is prepared from its lactam (Ann. **312**, 185).

δ-Amino-*n*-octoic acid, *homoconiinic acid,* $C_3H_7CH(NH_2)[CH_2]_3CO_2H$, m.p. 158°. The benzoyl compound is obtained by oxidation of benzoylconiine with $KMnO_4$ (Ber. **19**, 504).

ε-Aminocaproic acid, *ε-leucine,* $NH_2[CH_2]_5CO_2H$, m.p. 204°, is obtained from phthalimidobutylmalonic ester, from ε-benzoylaminocapronitrile, $C_6H_5\text{-}CONH[CH_2]_5CN$ (Ber. **40**, 1839), or from its lactam, obtained from *cyclo*hexanone oxime, by boiling with hydrochloric acid. ε-Aminocaproic acid is oxidized by permanganate to adipic acid ; nitrous acid produces two isomeric hexenoic acids instead of the expected ε-hydroxycaproic acid (p. 429) (Ann. **343**, 44).

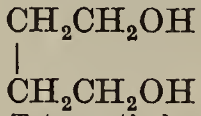
ζ-Amino-*n*-heptoic acid, $NH_2[CH_2]_6COOH$, m.p. 187° (decomp.), is also prepared from its lactam, suberone oxime (*q.v.*) ; also from the phthalimidoamylmalonic ester, or benzoylaminoamylmalonic ester (Ber. **40**, 1840). On heating, it does not yield a simple lactam (Ber. **35**, 1369). Permanganate oxidizes it to pimelic acid (Ber. **343**, 44).

ι-Aminocapric acid, $NH_2[CH_2]_9COOH$, m.p. 188°, is prepared from azelaic monoamido-acid, $NH_2CO[CH_2]_9COOH$, and alkali hypobromite ; *benzoyl derivative,* m.p. 97°. These products are not identical with those obtained from benzoyl decamethylene imine by oxidation (C. 1906, II. 1126).

Lactams (*Cyclic amides of the γ-, δ-, ε-, and ζ-amino acids*)

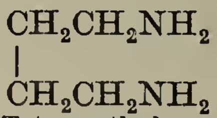
These cyclic amides are formed when the γ-, δ-, and ε-amino-acids are heated to their point of fusion, when they then lose water, and undergo an intramolecular condensation. Some of them have been obtained by the reduction of the anil chlorides of dibasic acids —*e.g.* succinimide and dichloromalein anil chloride. The names *γ-lactams* and *δ-lactams* recall the lactones. Just as the lactones, under the influence of the alkali hydroxides, yield hydroxy-acid salts, so the lactams, when digested with alkalis or acids, pass into salts of the amino-acids, from which they can be formed on the application of heat.

Further, the lactams bear the same relation to the imines of the alkylenediamines as the lactones to the oxides of the glycols (p. 367). These relations are apparent in the following arrangement :



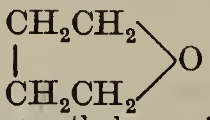
$$\begin{array}{l}CH_2CH_2OH\\ |\\ CH_2CH_2OH\end{array}$$

Tetramethylene glycol.



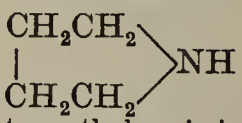
$$\begin{array}{l}CH_2CH_2NH_2\\ |\\ CH_2CH_2NH_2\end{array}$$

Tetramethylene diamine.



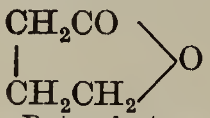
$$\left.\begin{array}{l}CH_2CH_2\\ |\\ CH_2CH_2\end{array}\right\rangle O$$

Tetramethylene oxide.
Tetrahydrofurfuran.



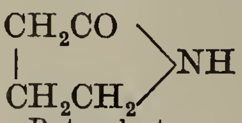
$$\left.\begin{array}{l}CH_2CH_2\\ |\\ CH_2CH_2\end{array}\right\rangle NH$$

Tetramethylene imine.
Tetrahydropyrrol.



$$\left.\begin{array}{l}CH_2CO\\ |\\ CH_2CH_2\end{array}\right\rangle O$$

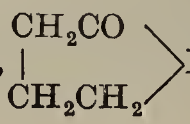
γ-Butyrolactone.

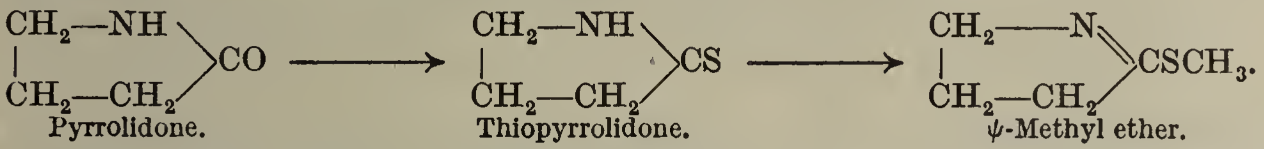


$$\left.\begin{array}{l}CH_2CO\\ |\\ CH_2CH_2\end{array}\right\rangle NH$$

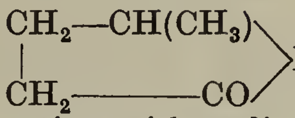
γ-Butyrolactam.
γ-Pyrrolidone.

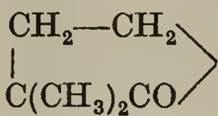
The amino-acids are not poisonous, but the γ- and δ-lactams are violent, strychnine-like poisons, affecting the spinal cord and producing convulsions. These bodies will be met with again among the pyrrole and pyridine derivatives, as tetrahydropyrrole and piperidine compounds (Vol. III).

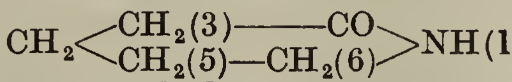
γ-Lactams : *γ-Butyrolactam, 2-pyrrolidone,*  $\left.\begin{array}{l}CH_2CO\\ |\\ CH_2CH_2\end{array}\right\rangle NH$, m.p. 25°, b.p. 245°, unites with water to form a crystalline *hydrate*, $C_4H_7ON + H_2O$, m.p. 35°. It is best prepared from succinimide by electrolytic reduction (Ber. **33**, 2224). *N-iso-Propyl-2-pyrrolidone*, $C_4H_6ON{\cdot}C_3H_7$, b.p. 222°, is similarly prepared from *iso*-propylsuccinimide, and *N-phenylbutyrolactam*, $C_4H_6ON{\cdot}C_6H_5$, from succinanil. It can also be produced by reduction of dichloromalein anil dichloride (Ann. **295**, 27). Pyrrolidone possesses feebly basic and acid properties. Its sodium salt reacts with iodomethane, producing *N-methylpyrrolidone*, $C_4H_6O{\cdot}NCH_3$, an oil. When boiled with P_2S_5 in xylol, pyrrolidone is converted into *thiopyrrolidone*, C_4H_7SN, the potassium salt of which, with iodomethane, gives *thiopyrrolidone ψ-methyl ether*, b.p. 170° (Ber. **40**, 2831, 2848):



The ψ-methyl ether, on reduction, breaks up into methyl mercaptan and pyrrolidine (p. 386).

γ-Valerolactam, 5-methyl-2-pyrrolidone,  m.p. 37°, can be distilled without decomposition. By reduction with sodium and amyl alcohol it is changed into 2-methylpyrrolidine (p. 386) (Ber. **23**, 1860, 2364, 3338 : **23**, 708).

3 : 3-*Dimethylpyrrolidone, αα-dimethylbutyrolactam*,  m.p. 66°, b.p. 237° (C. 1899, I. 874).

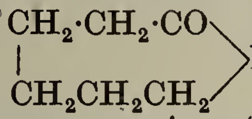
δ-Lactams : *δ-valerolactam, α-piperidone*,  m.p. 39–40°, b.p. 256°, is obtained, amongst other methods, by the isomerization of *cyclo*pentanone oxime (Ann. **312**, 179).

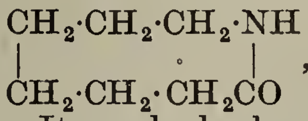
α-Methyl-δ-valerolactam, 3-methyl-2-piperidone, m.p. 55°, is isomeric with the β- or γ-methyl piperidone, m.p. 87°, obtained from β-methyl*cyclo*pentanone oxime (Ann. **312**, 186).

α-Ethyl-δ-valerolactam, 3-ethylpiperidone, m.p. 68°, b.p. 141°/42 mm. (Ber. **23**, 3694).

α-Propyl-δ-valerolactam, 3-propylpiperidone, m.p. 59°, b.p. 274°.

δ-n-Octanolactam, homoconiinic acid lactam, 6-propyl-2-piperidone, m.p. 84°.

ε-Caprolactam,  m.p. 69°, is obtained by the transformation of *cyclo*hexanone oxime (Ann. **312**, 187) ; and from ε-aminocaproic acid (p. 449). It acts, physiologically, as a nerve poison. β-Methyl*cyclo*hexanone oxime and also oximes of the terpene ketones, menthone and tetrahydrocarvone can be converted into two *methyl-ε-caprolactams*, m.pp. 44° and 105° (structure, Ann. **346**, 253), and two isomeric *methyl*iso*propyl-ε-caprolactams, menthone* iso*oxime*, m.p.. 120°, and *tetrahydrocarvone* iso*oxime*, m.p. 104° (Ann. **312**, 197, 203).

ζ-Heptolactam,  $\begin{array}{l} CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NH \\ | \qquad\qquad\qquad\quad | \\ CH_2{\cdot}CH_2{\cdot}CH_2CO \end{array}$, m.p. 25°, b.p. 156°/8 mm., is prepared from suberone oxime. It can be broken down into ζ-aminoheptoic acid (p. 450) which on warming with nitrous acid is converted into εζ-heptenoic acid (Ann. **312**, 205).

11. **Nitramino-fatty acids.** *Nitraminoacetic acid*, $CO_2HCH_2{\cdot}NHNO_2$, m.p. 103°, is prepared by hydrolysing its *ethyl ester* (m.p. 24°), which results on treating nitrourethane acetic ester, $C_2H_5O_2C{\cdot}N(NO_2){\cdot}CH_2CO_2C_2H_5$, with ammonia (Ber. **29**, 1682).

12. *iso***Nitramino-fatty acids** are obtained in the form of their sodium salts when sodium *iso*nitramino acetoacetic esters and sodium *iso*nitramino mono-alkylacetoacetic esters, or the explosive dinitroso-compounds of the hydrazo-fatty acids, such as hydrazo*iso*butyric acid (p. 452), are acted on by the alkalis (Ber. **29**, 667 : Ann. **300**, 64). They are converted into hydroxylamino-fatty acids by dilute mineral acids (p. 434). Acid reducing agents change

them to amino-fatty acids, whilst alkaline reducing agents produce diazo-acids (p. 458) and hydrazino-acids (see below).

iso*Nitraminoacetic acid*, $CO_2HCH_2N\!<\!\genfrac{}{}{0pt}{}{NO}{OH}$, is a syrupy liquid. iso*Nitramino*iso*butyric acid*, $CO_2HC(CH_3)_2\cdot N(NO)OH$, m.p. 94°. Their lead salts dissolve with difficulty (Ann. **300**, 59).

13 (*a*). **Hydrazino-fatty acids** are obtained, together with the diazo-acids, when the *iso*nitramino-fatty acids are acted on with alkaline reducing agents. Their carbamide derivatives are obtained in the form of nitriles when hydrocyanic acid becomes added to the ketone semicarbazones.

Hydrazinoacetic acid, $NH_2NH\cdot CH_2COOH$, m.p. 152°, with decomposition (Ber. **31**, 164). (See also Amidohydantoic ester and Carbamidohydrazo-acetic ester.)

α-*Hydrazinopropionic acid*, $NH_2NH\cdot CH(CH_3)CO_2H$, m.p. 180°, is formed from α-*iso*nitraminopropionic acid (Ber. **29**, 670), and from the addition product of hydrocyanic acid and acetaldehyde semicarbazone (Ann. **303**, 79).

α-*Hydrazino*iso*butyric acid*, $NH_2NH\cdot C(CH_3)_2CO_2H$, m.p. 237° (decomp.). It is formed when steam acts on its benzal derivative. The latter is made by acting on acetone semicarbazone, $NH_2CONHN{=}C(CH_3)_2$, with hydrocyanic acid, when carbamido-hydrazino-*iso*butyronitrile is produced. This is then decomposed with hydrochloric acid, and benzaldehyde is added (Ann. **290**, 15).

13 (*b*). **Hydrazo-fatty acids.**—When a hydrazino-fatty acid is treated with acetone and potassium cyanide, a hydrazo-nitrile acid results: thus, from α-hydrazino-*iso*butyric acid we get *hydrazo*-iso*butyric acid seminitrile*, $\genfrac{}{}{0pt}{}{(CH_3)_2}{HO_2C}\!\geqslant\! C\cdot NHNH\cdot C\!\leqslant\!\genfrac{}{}{0pt}{}{(CH_3)_2}{CN}$, m.p. 100°. When hydrazine sulphate (1 mol.), acetone (2 mols.), and potassium cyanide (2 mols.) react, the product is *hydrazo*-iso*butyronitrile*, $\genfrac{}{}{0pt}{}{(CH_3)_3}{NC}\!\geqslant\! C\cdot NH\cdot NH\cdot C\!\leqslant\!\genfrac{}{}{0pt}{}{(CH_3)_2}{CN}$, m.p. 92°. Hydrochloric acid converts both nitriles into *hydrazo*-iso*butyric acid*, $\genfrac{}{}{0pt}{}{(CH_3)_2}{HOOC}\!\geqslant\! C\cdot NHNH\cdot C\!\leqslant\!\genfrac{}{}{0pt}{}{(CH_3)_2}{COOH}$, m.p. 223°.

Its dinitroso-compound is decomposed by alkalis into *iso*nitramino*iso*butyric acid (see above), α-hydroxy-*iso*butyric acid and nitrogen (Ann. **300**, 59).

14. **Azo-fatty acids.**—Bromine water oxidizes hydrazo-esters and hydrazonitriles to the corresponding azo-bodies. *Azo*-iso*butyronitrile*, $\genfrac{}{}{0pt}{}{(CH_3)_2}{NC}\!\geqslant\! C\cdot N:N\cdot C\!\leqslant\!\genfrac{}{}{0pt}{}{(CH_3)_2}{CN}$, m.p. 105°, when heated alone, or, better, with hot water, passes into tetramethyl succinic nitrile (Ann. **290**, 1).

B. UNSATURATED HYDROXY-ACIDS, HYDROXY-OLEFINE CARBOXYLIC ACIDS

α-Hydroxy-olefine carboxylic acids are obtained by the action of cold hydrochloric acid on the nitriles, the addition products of hydrocyanic acid and olefine-aldehydes.

Vinylglycollic acid, $CH_2:CHCH(OH)COOH$, m.p. 33°, b.p. 129°, is prepared from its *nitrile, acrolein cyanohydrin*, b.p. 94°/17 mm., or the *amide*, m.p. 86°, b.p. 155–158°/21 mm. When heated with acids it is partly converted into the α-keto-acid—propionylformic acid, $CH_3CH_2CO\cdot COOH$. This also results, together with various condensation products, when vinyl glycollic acid is acted on by alkalis (Rec. trav. chim. **21**, 209).

Propenylglycollic acid, α-hydroxy-Δ^{β}-pentenoic acid, $CH_3CH:CHCH(OH)\cdot COOH$, is obtained from crotonaldehyde cyanohydrin. Boiling dilute acids convert it directly into a γ-keto-acid—lævulinic acid (Ber. **29**, 2582):

$$CH_3CH:CH\cdot CH(OH)COOH \longrightarrow CH_3CO\cdot CH_2CH_2COOH.$$

α-*Ethoxy-acrylic acid*, $CH_2:C(OC_2H_5)\cdot CO_2H$, m.p. 62°, is obtained by hydrolysis of its *ethyl ester*, b.p. 180° (*cf.* Acetal of Pyroracemic Ester, p. 464) (Ber. **31**, 1020).

β-Hydroxy-olefine carboxylic acids are obtained by condensation of olefine aldehydes with α-halogen-fatty esters by means of zinc (*cf.* mode of formation **12*a***, p. 411). When an available hydrogen atom is present in the α-position, these acids readily lose water, as when, for instance, they are boiled with sodium hydroxide, forming di-olefine carboxylic acids (Ber. **35**, 3633, C. 1903, II. 555: 1906, II. 318):

$$CH_3CH : CH\cdot CHO \xrightarrow[Zn]{Br\cdot CH_2CO_2R} \underset{\beta\text{-Hydroxy-hydrosorbic acid.}}{CH_3CH : CH\cdot CH(OH)CH_2CO_2R}$$

$$\longrightarrow \underset{\text{Sorbic acid.}}{CH_3CH : CH\cdot CH : CHCO_2H.}$$

β-Hydroxy-hydrosorbic acid is an oil, slightly soluble in water; *ethyl ester*, b.p. 100°/2 mm. *α-Methyl hydroxy-hydrosorbic ester*, b.p. 111°/15 mm. *α-Ethyl-β-hydroxysorbic ester*, b.p. 111°/15 mm. *α-Ethyl-β-hydroxy-hydrosorbic ester*, $CH_3CH : CHCH(OH)C(CH_3)_2CO_2R$, b.p. 119°/17 mm., is stable.

β-Hydroxy-αα-dimethyl-Δ^γ-pentenoic acid, *vinylhydroxypivalic acid*, $CH_2 : CH\cdot CH(OH)C(CH_3)_2CO_2H$, b.p. 159°/23 mm.; *ethyl ester*, b.p. 106°/19 mm., is prepared from acrolein, bromo*iso*butyric ester and zinc. In benzene solution, P_2O_5 causes the splitting off of water, and simultaneously the addition of benzene, forming the compound $C_6H_5\cdot CH_2CH : CHC(CH_3)_2CO_2R$;

β-Hydroxy-acrylic acid, $CH(OH) : CHCO_2H$, and *β-Hydroxycrotonic acid*, $CH_3C(OH) : CH\cdot CO_2H$. These acids and their homologues are the *aci-* or *enol-*forms (p. 456) of the β-aldo- and β-keto-carboxylic acids, such as formylacetic ester and acetoacetic ester:

enol-form	$CH(OH) : CHCO_2C_2H_5$	$CH_3C(OH) : CH\cdot CO_2C_2H_5$
keto-form	$CHO\cdot CH_2CO_2C_2H_5$	$CH_3CO\cdot CH_2CO_2C_2H_5.$
	Formyl acetic ester.	Acetoacetic ester.

In the free state formyl acetic ester exists as β-hydroxy-acrylic ester (*enol*-modification), whilst acetoacetic ester is more stable in the *keto*-form. Since the aci- or enol-form is usually looked on as being a subsidiary form, and the aldo- or keto-form, the fundamental modification, those derivatives, such as β-alkoxy- and β-acyloxy-olefine carboxylic acids, which are undoubtedly of the enol-form, will be described with the latter.

γ- and **δ-Hydroxy-olefine carboxylic acids** are known in the form of their lactones, of which some are obtained by distillation of the γ-keto acids, and others from βγ-dibromo- or dichloro-fatty acids with the loss of 2 molecules of halogen acid. These Δ^α- and Δ^β-lactones are changed back into γ-keto- or aldehyde acids by hydrolysis.

Δ^β-Butene lactone, crotolactone, $\overline{CH : CH\cdot CH_2COO}$, m.p. 4°, b.p. 96°/15 mm., is formed from βγ-dichlorobutyric acid when heated alone or with potassium carbonate (C. 1905, II. 45: Ber. **35**, 942).

γ-Ethoxycrotonic acid, $C_2H_5OCH_2CH : CHCOOH$, m.p. 45°, b.p. 148°/26 mm., is obtained from γ-ethoxy-β-hydroxybutyronitrile, the addition product of hydrocyanic acid to epiethylin, $C_2H_5OCH_2\overline{CH\cdot CH_2O}$ (C. 1905, I. 1138).

Δ^β-Angelic lactone, $CH_3\overline{C{=}CHCH_2COO}$, m.p. 18°, b.p. 167°, and *Δ^α-angelic lactone*, $CH_3\overline{CH\cdot CH : CHCOO}$, b.p. 83°/25 mm., are prepared from lævulinic acid and acetyl lævulinic acid. The Δ^β-lactone can be formed from the Δ^α-lactone by various methods; the change is, however, reversible. The Δ^β-lactone, in contradistinction to the Δ^α-lactone, can be condensed with aldehydes at the α-CH_2 group (Ann. **319**, 180).

Mesitonic acid (αα-dimethyl lævulinic acid, p. 479) gives rise to *α-dimethyl Δ^α-angelic lactone*, m.p. 24°, b.p. 167°. The isomeric *αα β-trimethyl-Δ^β-butenolactone* is prepared from the corresponding dibromo-acid. iso-*Octenolactone*, $(CH_3)_2CHCH_2\overline{CH\cdot CH : CH\cdot COO}$, is obtained from *iso*-octenoic acid dibromide (C. 1905, II. 457: Ann. **347**, 132).

γ-Methyl- and *γ-ethyl-αβ-dichloro-* and *-αβ-dibromo-butene lactone* $R\cdot\overline{CH\cdot CX : CXCOO}$, b.p. 120°/22 mm., b.p. 110°/4 mm.; m.p. 69°; m.p. 51°, are prepared from mucochloric acid and mucobromic acid (p. 457) by means of magnesium alkyl halides (Ber. **38**, 3981).

Parasorbic acid, or *sorbin oil,* $CH_3CH_2\overline{CHCH:CHCOO}$, or $CH_3\overline{CHCH_2CH:CHCOO}$, b.p. 221°, occurs, together with malic acid, in the juice of ripe and unripe mountain ash berries (*Sorbus aucuparia*). It is optically active: $[\alpha = +40{\cdot}8$, and is a strong emetic. It passes into sorbic acid (p. 353) when heated with sodium hydroxide or hydrochloric acid (Ber. **27**, 344).

Di-olefine δ-lactones have been obtained from *coumalinic acid* and iso*dehydracetic acid* by the splitting-off of carbon dioxide:

Coumalin, $\overline{CH{=}CH{-}CH{=}CH{\cdot}COO}$, m.p. 5°, b.p. 120°/30 mm., has an odour like that of coumarin (Ann. **264**, 293).

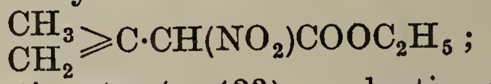
Mesitene lactone, βδ-Dimethylcoumalin, $CH_3\overline{C{=}CH{-}C(CH_3){=}CH{\cdot}COO}$, m.p. 51·5°, b.p. 245°. When heated with ammonia it changes to the corresponding lactam, so-called pseudo-*lutidostyril, mesitene lactam* (below).

Diallylbutyrolactone, $(CH_2:CHCH_2)\overline{CCH_2CH_2COO}$, b.p. 267°, is prepared from succinic ester, allyl iodide, and zinc (*cf.* the general method of formation of *tert.*-α-hydroxy-acid esters from oxalic ester, alkyl halides, and zinc, p. 411) (J. pr. Chem. [2] **71**, 249).

Ambrettolic acid, *Δ^{ζ}-o-hydroxyhexadecenoic acid,* $C_{16}H_{30}O_2$, $HO{\cdot}[CH_2]_7{\cdot}CH:CH{\cdot}[CH_2]_5{\cdot}COOH$, m.p. *c.* 25°, occurs in musk-kernel oil. Its lactone, *ambrettolide,* is one of the odoriferous principles of vegetable musk (Ber. **60**, 902).

Ricinoleic acid, $CH_3{\cdot}[CH_2]_5{\cdot}CH(OH){\cdot}CH_2{\cdot}CH:CH{\cdot}[CH_2]_7{\cdot}COOH$, has already been dealt with (p. 354).

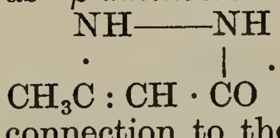
Nitro- and Amino-olefine Carboxylic Acids

α-Nitro-dimethylacrylic acid, $(CH_3)_2C:C(NO_2)COOH$. Its *ester,* b.p. 121°/24 mm., is prepared by nitrating dimethylacrylic ester (p. 346) with fuming nitric acid. Alcoholic potassium hydroxide converts it into the potassium salt of an *isomeric nitro-acid ester,*  $\begin{matrix}CH_3\\CH_2\end{matrix}\!\!>C{\cdot}CH(NO_2)COOC_2H_5$; ammonia decomposes it into acetone and nitro-acetic ester (p. 433); reduction with aluminium amalgam produces:

α-Aminodimethylacrylic ester, $(CH_3)_2C:C(NH_2)COOC_2H_5$, b.p. 94°/18 mm., is converted by hydrochloric acid into dimethyl pyroracemic acid (p. 464).

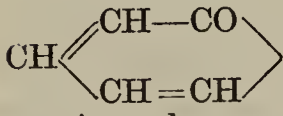
β-Amino-acids and β-Hydrazino Olefine Carboxylic Acids.

This group contains the reaction-products of ammonia and the hydrazines on β-ketone-acid esters such as acetoacetic esters and alkyl acetoacetic esters, such as *β-aminocrotonic ester,* $CH_3C(NH_2):CH{\cdot}CO_2C_2H_5$, and *methyl pyrazolone,*

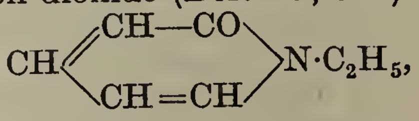


These behave desmotropically, and because of their close connection to the β-ketone-acid esters will be considered with them (p. 466).

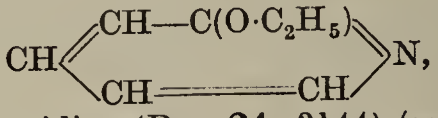
δ-Diolefine Lactams. *α-Pyridone, δ-aminopentadienoic acid lactam,*



m.p. 106°, is obtained from the reaction-product of ammonia and coumalic acid after the elimination of carbon dioxide (Ber. **18**, 317). It can be converted into the odourless *ethylimide,*

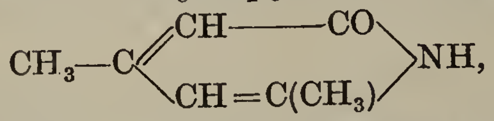


b.p. 258°, and *α-ethoxypyridine,*



b.p. 156°, which possesses an odour like that of pyridine (Ber. **24**, 3144) (see Vol. III).

pseudo-*Lutidostyril, 3 : 5-Dimethyl-2-pyridone, mesitene lactam,*



m.p. 180°, b.p. 305°, is formed when ammonia acts on mesitene lactone, and from the two monocarboxylic acids of this lactam by the elimination of CO_2 (Ann. **259**, 168).

ALDEHYDE- AND KETO-ACIDS

8. ALDEHYDE-ACIDS, $CHO·C_nH_{2n}·COOH$

These compounds show simultaneously the reactions of an aldehyde and a carboxylic acid. Formic acid, the first member of the saturated fatty acid series, also shows aldehydic properties, to which attention was drawn when the acid was previously discussed. The best known of the aldehyde acids is glyoxylic acid, $CHO·COOH$.

Glyoxylic acid, *glyoxalic acid* [ethanal acid] $(HO)_2·CH·CO_2H$ or $HCO·CO_2H + H_2O$, was found by *Debus* (1856) among the products resulting from the oxidation of alcohol with nitric acid. It occurs in unripe gooseberries and other fruit, from which it disappears on the fruit ripening. Its formation and reactions are of significance in plant physiology (Ber. **25,** 800 : **35,** 2446 : **40,** 4943). Just as chloral hydrate is to be considered as trichloroethylidene glycol, $CCl_3CH(OH)_2$, so crystallized glyoxylic acid can be regarded as the glycol corresponding with the aldehydo-acid; $CHO·CO_2H$. The salts are derived from the dihydroxyl formula of glyoxylic acid ; hence it may be designated dihydroxy-acetic acid. Like chloral hydrate, glyoxylic acid in many reactions behaves like a true aldehyde (Ber. **25,** 3425). The esters of glyoxylic acid are derived from the aldehyde formula.

Formation.—(1) Glyoxylic acid, accompanied by glyoxal (p. 398) and glycollic acid (p. 414), is one of the oxidation products of alcohol, aldehyde and glycol.

(2) It is produced from the dihalogen acetic acids by heating to 230° with water (Ber. **25,** 714), by heating the silver salts with water (Ber. **14,** 578), or better, by the action of potassium acetate on dichloroacetic acid, whereby the diacetyl compound, $(CH_3·CO·O)_2CH·COOH$, is formed and yields glyoxylic acid on heating with water (Ann. **311,** 129).

(3) From hydrazi-acetic acid (see p. 460).

(4) By reduction of oxalic acid and its ester (*cf.* also Glycollic acid, p. 415).

(*a*) Electrolytic reduction of oxalic acid in sulphuric acid and with mercury cathode gives an 87% yield of glyoxylic acid (Ber. **37,** 3187) :

$$COOH·COOH + H_2 = COOH·CH(OH)_2.$$

(*b*) A similar reduction of oxalic esters produces glyoxylic esters (Ber. **37,** 3591).

(*c*) Reduction of oxalic esters with sodium amalgam in alcohol produces the alcoholates of glyoxylic esters, together with keto-malonic esters, desoxalic esters, and racemic esters (Ber. **40,** 4942).

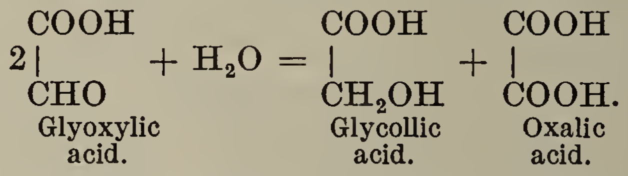
Properties.—It is a thick liquid, readily soluble in water, and crystallizes in rhombic prisms by long standing over sulphuric acid. The crystals have the formula $C_2H_4O_4$ (see above). It distils undecomposed with steam.

Salts.—The salts contain water of crystallization which, on being dried, they give up with partial decomposition. The *calcium salt*, $(C_2H_2O_3)_2Ca + 2H_2O$, is sparingly soluble in water (Ann. **317**, 147 : C. 1904, II. 1705).

Esters : Ethyl ester, $CHO{\cdot}COOC_2H_5$, b.p. 130°, an easily polymerized substance, is produced by the electrolytic reduction of oxalic ester, and also from its *alcoholate*, $C_2H_5OCH(OH)CO_2C_2H_5$, b.p. 137°, by the action of P_2O_5. This substance is prepared by the reduction of the oxalic ester with sodium amalgam (see above). Alcohol and hydrochloric acid produce *di-ethoxyacetic ester*, $(C_2H_5O)_2CHCO_2C_2H_5$, b.p. 199°, which, on hydrolysis, yields di-ethoxyacetic acid. Glyoxylic ethyl ester develops bright colorations with ammonia and methylamine in presence of air (C. 1906, I. 1654 : Ber. **40**, 4953). *Glyoxylic methyl ester*, m.p. 53° (Ber. **37**, 3591). Hydrazines, hydroxylamine, etc., give typical aldehyde derivatives with the esters (C. 1907, I. 401).

Reactions.—Glyoxylic acid exhibits all the properties of an aldehyde. It reduces ammoniacal silver solutions with formation of a mirror, and combines with primary alkali sulphites (p. 244), with phenylhydrazine (Ber. **17**, 577), with hydroxylamine, thiophenol and hydrochloric acid (Ber. **25**, 3426). When oxidized (silver oxide), it yields oxalic acid ; by reduction it forms glycollic acid and racemic acid, $CO_2HCH(OH){\cdot}CH(OH)COOH$.

On boiling the acid with alkalis, glycollic and oxalic acids are produced (Ber. **13**, 1931). This reaction is extramolecular, and completes itself by the intramolecular rearrangement of the first-formed glyoxal into glycollic acid :



$$2\begin{array}{l}COOH\\ |\\ CHO\end{array} + H_2O = \begin{array}{l}COOH\\ |\\ CH_2OH\end{array} + \begin{array}{l}COOH\\ |\\ COOH.\end{array}$$

Glyoxylic acid. Glycollic acid. Oxalic acid.

The formation of glycollic and tartaric acids also occurs when glyoxylic acid is carefully heated (C. 1904, II. 1705) ; they are also formed by the interaction of glyoxylic, hydrocyanic, and hydrochloric acids. Ammonia causes the elimination of CO_2 and the formation of formyl glycocoll (p. 442), and ultimately glycocoll (Ber. **35**, 2438). For the change of glyoxylic acid by urea into allantoin, see p. 627.

β-Aldo-carboxylic acids, $HOC{\cdot}CHR{\cdot}CO_2H$, and their esters exhibit reactions of *aci*-form compounds and behave as β-hydroxy-Δ^{α}-olefine carboxylic acids, $HOCH : CRCO_2H$ (p. 453), in which form they are most favourably constituted to yield esters.

Formylacetic acid, *β-aldopropionic acid, malonic acid semialdehyde,* $CHO{\cdot}CH_2COOH$ or $CH(OH) : CHCO_2H$, appears to be formed by the hydrolysis of its *acetal*, diethoxypropionic acid, $(C_2H_5O)_2CHCH_2COOH$. This is obtained by oxidation of β-hydroxypropionacetal (p. 390) (Ber. **33**, 2760) ; *ethyl ester*, b.p. 193° ; and also from orthoformic ester (p. 290), bromoacetic ester and zinc (J. pr. Chem. [2] **73**, 326) :

$$HC(OC_2H_5)_3 + BrZnCH_3COOC_2H_5 = HC(OC_2H_5)_2{\cdot}CH_2CO_2C_2H_5 + C_2H_5OZnBr.$$

It readily loses alcohol, forming the ester of *β-ethoxyacrylic acid*, $C_2H_5OCH : CHCOOH$, m.p. 110°. This readily decomposes into CO_2 and acetaldehyde, probably with the intermediate formation of formylacetic acid.

Formylacetic ester, hydroxymethyleneacetic ester, β-hydroxyacrylic ester, $(C_2H_3O)CO_2R$, is obtained in the form of its *sodium* compound, $NaOCH : CHCO_2R$, by the condensation of formic and acetic esters by means of sodium in benzene or ethereal solution :

$$HCOOC_2H_5 + CH_3COOC_2H_5 + Na = NaOCH : CHCOOC_2H_5 + HOC_2H_5.$$

The free ester is easily condensed to formylglutaconic ester, $HC(OH) : C(CO_2R)CH : CH{\cdot}CO_2R$, and trimesic ester, $C_6H_3(CO_2R)_3$. Concentrated sulphuric acid produces coumalic acid (*q.v.*). Acetyl chloride and sodium formylacetic ester form an *acetate*, $CH_3CO\cdot OCH : CHCO_2C_2H_5$, b.p. 126°/46 mm. This takes up 2 atoms of bromine producing a *dibromide*, b.p. 154°/34 mm., which indicates the structure of the acetate (Ber. **25**, 1046). Nitrobenzoyl chloride produces two stereoisomeric *nitrobenzoates* (Ann. **316**, 18). Cyanoacetaldehyde, hydroxymethyleneacetonitrile, $HO\cdot CH : CH\cdot CN$, is produced as a sodium salt from isoxazole and sodium ethoxide (p. 407).

α-Formylpropionic acid, *α-hydroxymethylenepropionic acid,* $OCHCH(CH_3)CO_2H$ or $CH(OH) : C(CH_3)CO_2H$; its *acetal,* $(C_2H_5O)_2CH\cdot CH(CH_3)CO_2H$, of which the ester is prepared from orthoformic ester and α-bromopropionic acid by means of zinc, easily breaks down into alcohol and *β-ethoxymethacrylic acid,* $C_2H_5OCH : C(CH_3)CO_2H$, m.p. 109°. This is formed from bromo-methacrylic acid and sodium ethoxide. It readily decomposes into CO_2, propionaldehyde and alcohol (Ber. **39**, 3549). *α-Formylpropionic ester,* $HOCH : C(CH_3)CO_2C_2H_5$, b.p. 161° ; *acetate,* b.p. 132°/48 mm. (Ann. **316**, 333).

γ- and δ-Aldo-carboxylic Acids.

β-Formylpropionic acid, γ-aldobutyric acid (semialdehyde of succinic acid), $CHO\cdot CH_2\cdot CH_2CO_2H$, is produced from acetal malonic acid $(C_2H_5O)_2CH\cdot CH_2CH(CO_2H)_2$, when the latter is heated with water to 190° ; or, better, by boiling aconic acid (*q.v.*) in water, when CO_2 is given off (Ber. **37**, 1801). It forms crystals, soluble in water. When evaporated with sodium hydroxide solution, it yields a small quantity of terephthalic acid (Vol. II) ; reduction converts it into butyrolactone. Its *nitrile-acetal,* $CN\cdot CH_2\cdot CH_2CH(OEt)_2$, b.p. 106°/45 mm., is obtained from β-chloropropionacetal and KNC (Ber. **34**, 1924).

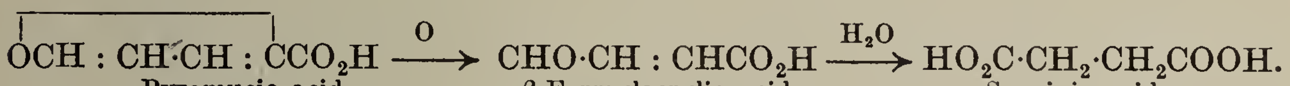
*β-Formyl*iso*butyric acid,* $CHO\cdot CH_2CH(CH_3)CO_2H$ (C. 1899, I. 557).

δ-Aldovaleric acid, γ-formylbutyric acid (semialdehyde of glutaric acid), $CHO\cdot CH_2CH_2CH_2COOH$, b.p. 240°, is prepared from β-propionacetal malonic ester by hydrolysis and the loss of CO_2 (Ber. **38**, 2884) ; by boiling the ozonide of *cyclo*pentene (Vol. II) with water, associated with *glutaric dialdehyde,* b.p. 71°/10 mm. (p. 400) and glutaric acid (Ber. **41**, 1706).

δ-Formyl-γ-methylvaleric acid, $HOC\cdot CH(CH_3)CH_2CH_2COOH$, b.p. 154°/12 mm., is obtained by the oxidation of citronellal acetal (p. 255) with permanganate (Ber. **34**, 1498).

Unsaturated Aldehyde Acids.

β-Formylacrylic acid (semialdehyde of maleic acid), $CHOCH : CHCOOH$, m.p. 55°, b.p. 145°/10 mm., is produced by the oxidation of pyromucic acid (Vol. II) by bromine and alkali. It is converted into succinic acid when heated with a solution of potassium cyanide (Ber. **38**, 1272) :

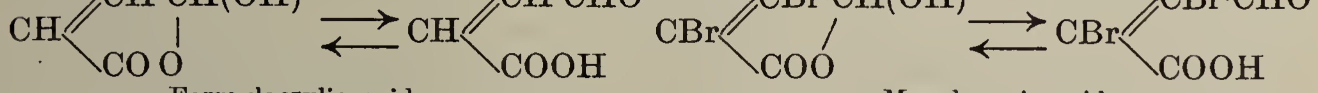


$$OCH : CH\cdot CH : CCO_2H \xrightarrow{O} CHO\cdot CH : CHCO_2H \xrightarrow{H_2O} HO_2C\cdot CH_2\cdot CH_2COOH.$$

Pyromucic acid. β-Formylacrylic acid. Succinic acid.

By the energetic action of chlorine and bromine on pyromucic acid, halogen derivatives of formylacrylic acid are produced—*mucochloric acid,* m.p. 125°, and *mucobromic acid,* m.p. 122°.

Similarly to the γ-keto-acids (p. 477), these acids can be looked on as being hydroxylactones, with which they are tautomeric (Monatsh. **25**, 492) :



Formylacrylic acid. Mucobromic acid.

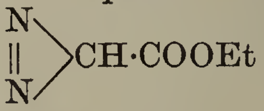
The *esters* of mucochloric and mucobromic acids, which, unlike the acid, do not yield oximes, appear to be derived from the lactone formula ; there are, however, also esters which have been obtained from the normal aldehyde-acid.

Nitrogen Derivatives of the Aldehyde-acids

Dinitro-acetic ester, $(NO_2)_2CHCO_2C_2H_5$, is prepared from malonic ester and fuming nitric acid. It is a colourless liquid, which cannot be distilled without decomposition. It reacts strongly acid.

Diaminoacetic acid, $(NH_2)_2CHCOOH$, is unknown. A derivative, *tetramethyldiaminoacetic methyl ester,* $[(CH_3)_2N]_2CHCOOCH_3$, b.p. 57°/12 mm., is obtained from diiodoacetic ester and dimethylamine. Dibromoacetic ester, by the same reaction, yields *hydroxy-dimethylaminoacetdimethylamide*, $(CH_3)_2NCH(OH)CON(CH_3)_2$, b.p. 80°/12 mm. (Ber. **35**, 1378).

Diazoacetic acid, $N_2CH\cdot COOH$, is unstable in the free state, but its *ethyl ester* is the most important of the aliphatic diazo-compounds. Though they show some similarities to the aromatic diazo-compounds, they must also be compared with the ketens, carbylamines, azides, etc.

Two formulæ have been considered for the aliphatic diazo-compounds. Curtius, the discoverer, suggested the formula  $\overset{N}{\underset{N}{\|}}\!>CH\cdot COOEt$ for diazoacetic ester. More recently an open chain formula has been suggested, due to Angeli-Thiele, $N \vdots N : CH\cdot COOEt$. Staudinger has brought forward support for the open chain *diazene* formula (Helv. Chim. Acta. **5**, 87) and the optical properties also furnish support (*Lardy*, J. Chim. phys. **21**, 281) (*cf.* Diazo-compounds, p. 251).

(1) The esters of the diazo-acids result when potassium nitrite acts on the hydrochlorides of the amino-fatty acid esters (p. 439) (*Curtius*, Ber. **29**, 759):

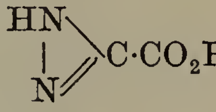
$$\underset{\text{Glycocoll ester hydrochloride.}}{HCl\cdot(H_2N)CH_2CO_2C_2H_5} + KNO_2 = \underset{\text{Diazoacetic ester.}}{N_2 : CHCO_2C_2H_5} + KCl + 2H_2O.$$

The higher amino-esters, containing an asymmetric carbon atom, yield by this method optically active diazo derivatives.

The di- and poly-peptide ester hydrochlorides, which contain the NH_2CH_2CO-group, behave with alkali nitrites in the same way as glycocoll ester hydrochloride: highly crystalline diazo-esters are formed, such as *diazoacetylglycine ester*, $N_2CH\cdot CONHCO_2C_2H_5$, m.p. 187°, as yellow crystals. The homologous α-amino-acids, such as alanine, leucine, also yield diazo-esters, if somewhat less readily; but β- and γ-amino-esters give hydroxy-esters instead of diazo-compounds (Ber. **37**, 1263).

(2) The sodium salts of the diazo-acids are prepared by reduction of the *iso*-nitramine fatty acids (p. 451) by means of sodium amalgam (Ber. **29**, 667):

$$HO_2N_2CH_2CO_2Na + 2H = 2H_2O + N_2 : CH\cdot CO_2Na.$$

The diazoacetic esters are very volatile, yellow-coloured liquids, with a peculiar odour. They distil undecomposed with steam, or under reduced pressure. They are slightly soluble in water, but mix readily with alcohol and ether. Like aceto-acetic ester, they are feeble acids in which the hydrogen of their CHN_2-group can be replaced by alkali metals by means of anhydrous alcoholates. Isomerization occurs, and there are formed salts of iso*diazoacetic ester*,  $\overset{HN}{\underset{N}{|}}\!>C\cdot CO_2R$, which can be obtained as an unstable oil by careful precipitation. It can be differentiated from the true diazoacetic ester by the fact that warm acids do not liberate N_2 from it (p. 459), but decompose it into hydrazine and oxalic acid (Ber. **34**, 2506).

Aqueous alkalis gradually hydrolyse and dissolve diazoacetic ester, forming salts, $CHN_2\cdot CO_2M$, which are decomposed by acids, evolving nitrogen.

Sodium diazoacetate, yellow in colour, dissolves with extreme ease in water. The reaction of its solution is alkaline (Ber. **34**, 2521).

Ethyl diazoacetate, $N_2CHCO_2C_2H_5$, m.p. − 24°, b.p. 143°, $D_{22} = 1{\cdot}073$, explodes with violence when brought into contact with concentrated sulphuric acid. A blow does not have this effect. At temperatures near its boiling point it decomposes into nitrogen and fumaric ester. Its *mercury derivative*, $Hg(CN_2\cdot CO_2\cdot C_2H_5)_2$, m.p. 104°, with formation of froth, results when yellow mercuric oxide acts on well-cooled diazoacetic ester. It separates from ether in transparent, sulphur-yellow, rhombic crystals. Concentrated ammonia converts the ester, like all other esters, into an amide, *diazoacetamide*, $N_2CHCONH_2$, m.p. 114° with decomposition. When diazoacetic ester is reduced it breaks down into ammonia and glycocoll. *pseudo*- and *Bis-diazoacetamide* (see below). *Diazoacetonitrile*, $N_2CH\cdot COCN$, b.p. 46°/14 mm., is prepared from amino-acetonitrile hydrochloride (p. 441) and sodium nitrite (Ber. **31**, 2489). It is an orange-yellow, very mobile liquid, possessing a pleasant odour resembling acetonitrile, but which irritates the mucous membranes.

Higher diazo-fatty esters, see J.A.C.S., **44**, 1798.

The diazo-esters are very reactive compounds, either by the ready replacement of their two nitrogen atoms by two monovalent radicals, or by their ability to form new heterocyclic rings without loss of nitrogen by addition reactions or isomerization. A résumé of the reactions of the diazo-compounds is given by Staudinger (Helv. Chim. Acta, **5**, 87).

Reactions.—(1) The diazo-esters are converted on heating with water or dilute acids into esters of the hydroxy acids:

$$N_2CH{\cdot}COOEt + H_2O \longrightarrow HO{\cdot}CH_2{\cdot}COOEt + N_2.$$

This reaction serves for the quantitative determination of the nitrogen in diazo-compounds.

(2) Alkoxy-fatty acid esters are produced on boiling with alcohols; a small quantity of aldehyde is produced at the same time:

$$N_2CHCO_2C_2H_5 + C_2H_5OH = \underset{\text{Ethyl ethoxyacetate.}}{CH_2(OC_2H_5)CO_2C_2H_5} + N_2;$$

(3) Acid derivatives of the glycollic esters are obtained on heating the diazo-compounds with organic acids:

$$N_2CHCO_2C_2H_5 + \underset{\text{Acetic acid.}}{C_2H_3OOH} = \underset{\text{Aceto-glycollic ester.}}{CH_2(OC_2H_3O)CO_2H_5} + N_2.$$

(4) The halogen acids act, even in the cold, on the diazo-compounds. The products are halogen-fatty esters:

$$N_2CHCO_2C_2H_5 + HCl = CH_2ClCO_2C_2H_5 + N_2.$$

(5) The halogens produce esters of dihaloid fatty acids:

$$NCH_2CO_2C_2H_5 + I_2 = \underset{\text{Di-iodo-acetic ester.}}{CHI_2CO_2C_2H_5} + N_2.$$

Diazoacetamide is changed, in a similar manner, to di-iodo-acetamide, $CHI_2{\cdot}CO{\cdot}NH_2$. By titration with iodine it is possible to employ this reaction for the quantitative estimation of diazo-fatty compounds (Ber. **18**, 1285).

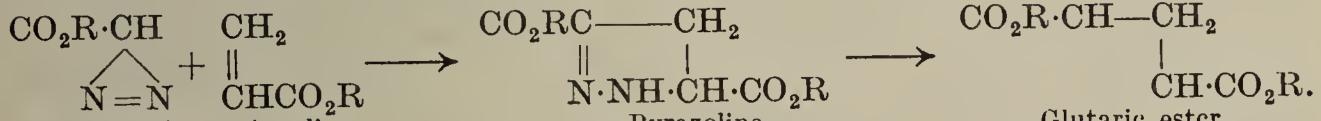
(6) The esters of anilino-fatty acids, $C_6H_5NH{\cdot}CH_2CO_2R$, result from the reaction of the anilines with diazo-esters.

(7) The esters of the diazo-fatty acids unite with aldehydes to form esters of the β-ketonic acids, *e.g.* benzoyl acetic ester, $C_6H_5CO{\cdot}CH_2CO_2C_2H_5$, trichloroaceto-acetic ester, $CCl_3COCH_2CO_2R$ (*cf.* p. 477) (Ber. **18**, 2379: **40**, 3000).

(8) Acid chlorides react with diazo-esters to form *C*-alkyl derivatives (Ber. **49**, 1978):

$$R{\cdot}CO{\cdot}Cl + CH(N_2){\cdot}COOEt \longrightarrow R{\cdot}CO{\cdot}C(N_2){\cdot}COOEt + HCl.$$

(9) Diazoacetic ester forms well-crystallizable addition products with unsaturated acid esters, such as acrylic, cinnamic, fumaric esters. Pyrazoline-carboxylic esters (Vol. III) are thus formed, which, on heating, lose nitrogen and are converted into glutaric esters:



Diazoacetic acid. Acrylic acid. Pyrazoline dicarboxylic ester. Glutaric ester.

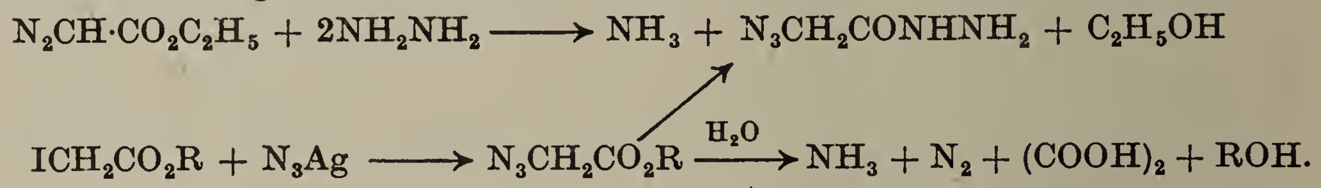
(10) Diazoacetic ester also reacts with benzene and its homologues, when heated with them, with loss of nitrogen and formation of dicyclic bodies, such as benzotrimethylene or norcaradiene carboxylic esters (Vol. II) (Ber. **29**, 108: **32**, 701: Ann. **358**, 1):

Benzene. *pseudo*Phenylacetic ester.

(11) Diazoacetamide is converted into triazolone when heated with barium hydroxide solution (Vol. III):

Diazoacetylglycinamide (see above) similarly yields triazoloneacetamide (Ber. **39**, 4140).

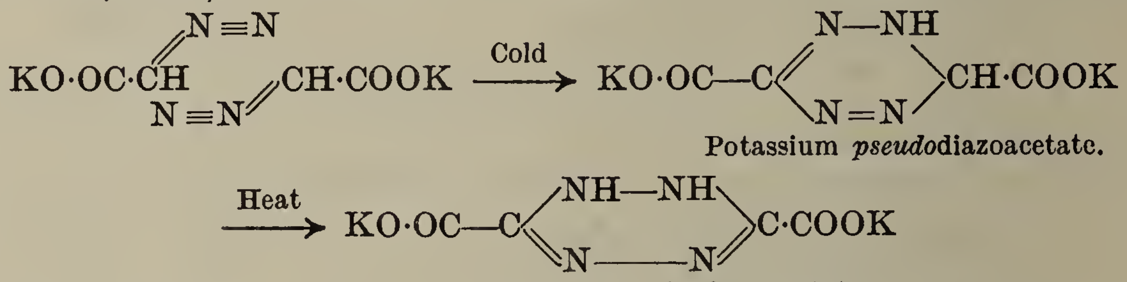
(12) Hydrazine and diazoacetic ester or diazoacetamide form the hydrazide of *azidoacetic acid*, $N_3CH_2CO_2H$, of which the *ethyl ester*, b.p. 75°/21 mm., is prepared also from iodoacetic ester and silver azide or chloroacetic ester and sodium azide. It is a colourless oil. Boiling alkalis decompose the acid into ammonia, nitrogen and oxalic acid (Ber. **41**, 344 : C. 1908, I. 938) :



$$N_2CH{\cdot}CO_2C_2H_5 + 2NH_2NH_2 \longrightarrow NH_3 + N_3CH_2CONHNH_2 + C_2H_5OH$$

$$ICH_2CO_2R + N_3Ag \longrightarrow N_3CH_2CO_2R \xrightarrow{H_2O} NH_3 + N_2 + (COOH)_2 + ROH.$$

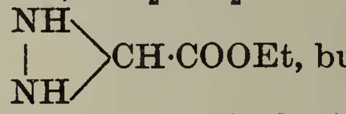
(13) With concentrated potassium hydroxide or liquid ammonia, in the cold, are obtained salts of the bimolecular so-called *pseudo*diazoacetic acid, *i.e.* 1 : 6-dihydro-1 : 2 : 4 : 5-tetrazine-3 : 6-dicarboxylic acid, whereas with heat the same reagents yield the salts of bisdiazoacetic acid, *i.e.* the 1 : 2-dihydrotetrazine derivative (Ber. **41**, 3161) :



Potassium *pseudo*diazoacetate.

Potassium bisdiazoacetate.

Breakdown of these compounds, with formation of tetrazines and triazoles, see *Curtius*, Ber. **41**, 3161.

(14) On reduction of diazoacetic ester followed by hydrolysis of the primary product, Curtius obtained hydrazine, $NH_2{\cdot}NH_2$. He regarded the intermediate compound as hydraziacetic ester,  but Staudinger (Helv. Chim. Acta. **4**, 228) has shown that the compound obtained by careful reduction, catalytically or by means of ammonium sulphide, of diazoacetic ester is the hydrazone of glyoxylic ester, which can be hydrolysed to glyoxylic acid and hydrazine by acids. This lends some support to the open chain formula for the diazo-compounds :

$$CH(N_2){\cdot}COOEt \longrightarrow NH_2{\cdot}N : CH{\cdot}COOEt \longrightarrow NH_2{\cdot}NH_2 + CHO{\cdot}COOH + EtOH.$$

(15) Phosphines, in particular triphenylphosphine $P(C_6H_5)_3$, unite with aliphatic diazo-compounds with formation of phosphazines (Helv. Chim. Acta. **5**, 75) :

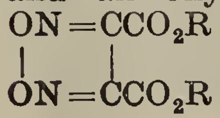
$$(C_6H_5)_3P + N ⋮ N : CH{\cdot}COOEt \longrightarrow (C_6H_5)_3P : N{\cdot}N : CH{\cdot}COOEt.$$

(16) Grignard reagents also add on readily, with formation of substituted hydrazones (Monatsh. **34**, 1609) :

$$R{\cdot}MgBr + CH(N_2){\cdot}COOEt \longrightarrow BrMg{\cdot}NR{\cdot}N : CH{\cdot}COOEt \longrightarrow NHR{\cdot}N : CH{\cdot}COOEt.$$

Oximes and Hydrazones of the Aldocarboxylic Acids

Oximinoacetic acid, isonitrosoacetic acid, glyoxylic oxime, HON : CH·COOH, m.p. 143° (decomp.), is prepared from glyoxylic acid and hydroxylamine ; from dichloro- or dibromoacetic acid, hydroxylamine and potassium hydroxide solution ; and from the hydrolysis of its ester. It forms colourless needles. *Ethyl ester*, m.p. 35°, b.p. 111°/12 mm., consists of deliquescent crystals ; *methyl ester*, m.p. 55°, b.p. 100°/15 mm. ; iso*butyl ester*, b.p. 118°/10 mm., can be prepared from acetoacetic ester by decomposition with nitrosyl sulphuric acid. Treatment with acetic anhydride converts *iso*nitrosoacetic ester into cyanoformic ester, $NC{\cdot}CO_2R$; N_2O_4, produces *iso*nitrosonitroacetic ester, $HONC(NO_2)CO_2R$, and an oily substance, probably a peroxide [of dioximinosuccinic ester :

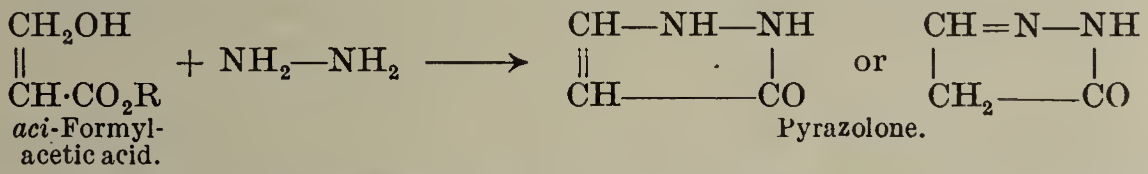


(*cf.* Ber. **28**, 1216 : **37**, 1530 : C. 1904, II. 195 ; 1907, I. 401).

β-Oximinopropionic acid, $HON : CHCH_2COOH$, m.p. 117° with decomposition, is prepared from coumalic acid and hydroxylamine (comp. p. 616) (Ann. **264**, 286 : Ber. **25**, 1904).

Glyoxylic acid phenylhydrazone, $C_6H_5NHN : CHCO_2H$, m.p. 137° (decomp.), is decomposed by nitrous acid into CO_2 and phenyl azoformaldoxime, $C_6H_5N : NCH : NOH$ (J. pr. Chem. [2] **71**, 366) ; *ethyl ester*, m.p. 131°, can be distilled under reduced pressure (C. 1907, I. 401).

Hydrazones of β-aldocarboxylic acids, such as of formylacetic acids, and their esters very easily part, intramolecularly, with water or alcohol, forming lactam-like bodies, known as pyrazolones (Vol. III). In order to indicate the lactam character of such substances, when the lactam-nitrogen is joined to a second nitrogen atom in the ring, they have been named *lactazams* :

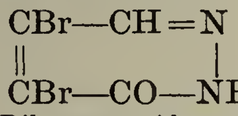

aci-Formyl-acetic acid.
Pyrazolone.

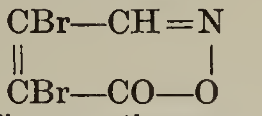
β-Ketocarboxylic acids (p. 466) also easily form γ-lactazams (pyrazolones).

Hydrazones of the γ- and δ-aldocarboxylic acids.

β-Formylpropionic acid ester phenylhydrazone is a non-crystallizable oil ; *phenylhydrazide*, $C_6H_5NHN : CHCH_2CH_2CONHNHC_6H_5$, m.p. 182°, is prepared from aconic acid (*q.v.*) and excess of phenylhydrazine. When warmed with sulphuric acid it yields indole-β-acetic acid (Ann. **339**, 373). Similarly, *formylbutyric acid phenylhydrazone*, $C_6H_5NHN : CHCH_2CH_2CH_2COOH$, yields indole-β-propionic acid, which is also formed from tryptophane by putrefaction (Ber. **38**, 2884).

Mucobromic acid (p. 457) and hydrazines form hydrazone anhydrides or δ-lactazams (Pyridazones, Vol. III) ; with hydroxylamine it gives an oxime anhydride (lactazone or orthoxazone, Vol III) (Ber. **32**, 534) :


Dibromopyridazone,
m.p. 224°.


Dibromo-orthoxazone,
m.p. 125°.

9. KETONE CARBOXYLIC ACIDS

These contain both the groups CO and CO_2H ; they, therefore, show acid and ketone characters with all the specific properties peculiar to both. In conformity with the scheme of nomenclature employed for the mono-substituted fatty acids and the various diketones (pp. 401–405), we distinguish the groups α-, β-, γ-, δ-, etc., among the ketocarboxylic acids :

The α-, γ-, and δ-, etc., acids are fairly stable in a free condition, whilst the β-acids are stable only in the form of esters, the free acids decomposing readily.

Nomenclature.—The ketonic acids are usually designated either as acyl derivatives of the fatty acids or as keto-substitution products of the fatty acids or oxofatty acids :

$CH_3{\cdot}CO{\cdot}CO_2H$	$CH_3{\cdot}CO{\cdot}CH_2CO_2H$	$CH_3{\cdot}CO{\cdot}CH_2CH_2CO_2H$
Acetylformic acid.	Acetoacetic acid.	β-Acetylpropionic acid.
α-Ketopropionic acid.	β-Ketobutyric acid.	γ-Ketovaleric acid.
(α-Oxopropionic acid).	(β-Oxobutyric acid).	(γ-Oxovaleric acid).

The "Geneva names" are formed by the addition of the word "acid" to the names of the ketones, as the ketonic acids may be considered as being the oxidation products of the latter.

CH_3COCO_2H	$CH_3CO{\cdot}CH_2CO_2H$	$CH_3COCH_2CH_2CO_2H$.
[Propanone acid].	[2-Butanone acid].	[3-Pentanone acid].

Formation.—The more stable α-, γ-, and δ-ketonic acids can be prepared by the oxidation of the secondary alcohol acids corresponding with them. Other methods will be given under the individual classes of these acids.

Reactions.—The ketone nature of these acids is shown by numerous reactions, *e.g.* nascent hydrogen converts the ketonic acids into the corresponding alcohol acids. They unite with alkali hydrogen sulphites, with hydroxylamine, and with phenylhydrazine.

A. SATURATED KETONE CARBOXYLIC ACIDS

I. α-Ketonic Acids.—$R{\cdot}CO{\cdot}CO_2H$

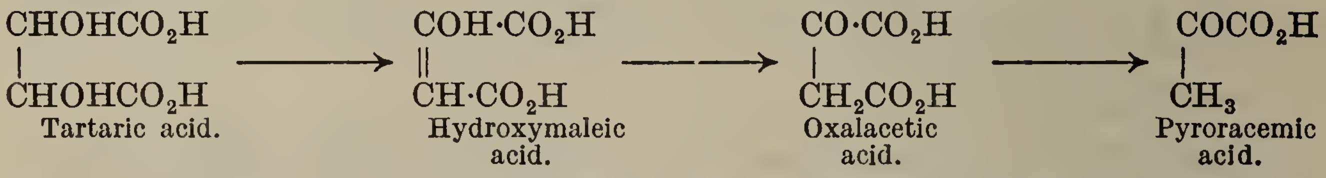
In this class the ketone group CO is in direct union with the acid-forming carboxyl group, CO_2H. We can look upon them as being compounds of acid radicals with carboxyl, or as derivatives of formic acid, $HCO{\cdot}OH$, in which the hydrogen linked to carbon is replaced by an acid radical. This view indicates, too, the general synthetic method of formation of these acids from (1) the cyanides of acid radicals (p. 464), which, by the action of concentrated hydrochloric acid, are changed to the corresponding ketonic acids:

$$CH_3{\cdot}CO{\cdot}CN + 2H_2O + HCl = CH_3{\cdot}CO{\cdot}CO_2H + NH_4Cl.$$

(2) A second general method of formation of α-ketonic acids and their esters consists in converting α-alkyl acetoacetic esters into the α-oximino-fatty acids (p. 465) and decomposing these with excess of nitrosyl sulphuric acid (C. 1904, II. 1706):

$$HON : CRCOOC_2H_5 \xrightarrow{HNO_2} O : CRCOOC_2H_5 + N_2O + H_2O.$$

Pyroracemic acid, *pyruvic acid,* [propanone acid], $CH_3{\cdot}CO{\cdot}CO_2H$, m.p. + 3°, b.p. 165–170°/760 mm. (decomp.), b.p. 61°/12 mm., was first obtained in the distillation of tartaric acid, racemic acid (*Berzelius,* 1835) and glyceric acid. (1) The acid is made by the distillation of tartaric acid alone (Ann. **172,** 142) or with potassium hydrogen sulphate (Ber. **14,** 321). We may assume that in this decomposition the first product is hydroxymaleic acid, which is converted into oxalacetic acid, which then gives up CO_2 to form pyroracemic acid:



$$\begin{array}{cccccccc} \begin{array}{l} CHOHCO_2H \\ | \\ CHOHCO_2H \end{array} & \longrightarrow & \begin{array}{l} COH{\cdot}CO_2H \\ \| \\ CH{\cdot}CO_2H \end{array} & \longrightarrow & \begin{array}{l} CO{\cdot}CO_2H \\ | \\ CH_2CO_2H \end{array} & \longrightarrow & \begin{array}{l} COCO_2H \\ | \\ CH_3 \end{array} \\ \text{Tartaric acid.} & & \text{Hydroxymaleic acid.} & & \text{Oxalacetic acid.} & & \text{Pyroracemic acid.} \end{array}$$

It is obtained from (2) α-dichloropropionic acid (p. 336), when heated with water; (3) in the oxidation of α-hydroxypropionic acid or ordinary lactic acid with potassium permanganate; (4) by the decomposition of oxalacetic ester; (5) from acetyl cyanide by the action of concentrated hydrochloric acid (p. 464); (6) by the oxidation of citraconic and mesaconic acid by $KMnO_4$.

(7) It may be obtained in 90% yield by the oxidation of methylglyoxal, $CH_3{\cdot}CO{\cdot}CHO$, with bromine water (Biochem. Z. **166,** 442).

Pyroracemic acid is a liquid, soluble in alcohol, water and ether, and has an odour quite similar to that of acetic acid. On boiling at atmospheric pressure it decomposes partially into CO_2 and pyrotartaric acid (*q.v.*). This change is more readily effected if the acid be heated to 100° with hydrochloric acid.

Pyruvic acid is the most important intermediate in the alcoholic fermentation of the hexoses. It is readily fermented by yeast (see p. 141). It is also of importance in the animal organism, both in the breakdown of complex substances, and in synthetic processes. (See Sugars, Proteins, Amino-acids: also Ann. **436,** 229: C. 1925, II. 728: Ber. **57,** 1436: J. Biol. Chem. **25,** 571.)

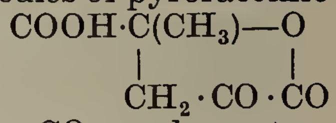
Reactions.—Pyruvic acid reduces ammoniacal silver solutions with formation of a silver mirror, the acid being converted into acetic acid and carbon dioxide. It is quantitatively decomposed into these substances by hydrogen peroxide (C. 1904, II. 194). When heated with dilute sulphuric acid to 150° it splits up into CO_2 and aldehyde, $CH_3{\cdot}COH$. This ready separation of aldehyde accounts for the ease with which pyroracemic acid enters into various condensations, *e.g.* the formation of crotonic acid by the action of acetic anhydride (p. 344) (Ber. **18,** 987: **19,** 1089), and the condensations with dimethylaniline and phenols in the presence of $ZnCl_2$. The acid condenses with the benzene hydrocarbons, in the presence of sulphuric acid, without decomposition (Ber. **14,** 1595: **16,** 2072). It condenses with acetone to form acetonedipyruvic acid (*q.v.*). A sensitive reaction for the detection of pyruvic acid depends upon its capacity to form substituted naphthocinchonic acids when condensed with β-naphthylamine and aldehydes (see Z. angew. Chem. **39,** 951).

Pyruvic acid forms crystalline compounds with the alkali hydrogen sulphites, in which it resembles the ketones. Nascent hydrogen (Zn and HCl, or HI) changes it to ordinary α-lactic acid, $CH_3CH(OH)CO_2H$, and dimethyl racemic acid (*cf.* Glyoxylic acid, p. 455). H_2S passed through pyroracemic acid produces *thiodilactic acid,* $S[C(CH_3)(OH){-}COOH]_2$, m.p. 94°, which is easily decomposed into its components (C. 1903, I. 16). Mercaptans, *e.g.* phenylmercaptan, combine with pyroracemic acid to form $CH_3C(OH)(SC_6H_5)CO_2H$ (Ber. **28,** 263). Pyroracemic ester, mercaptan and hydrochloric acid react together to form the *mercaptole,* $CH_3{\cdot}C(SC_2H_5)_2CO_2C_2H_5$, which on oxidation passes into the *sulphone,* $CH_3C(SO_2C_2H_5)_2CO_2C_2H_5$, m.p. 61° (Ber. **32,** 2804).

It reacts with phenylhydrazine and hydroxylamine to form a phenylhydrazone and an oxime (p. 465). The reaction with ammonia is described on p. 465. Hydrocyanic acid combines with pyruvic acid to form hydroxy*iso*succinic acid seminitrile.

The change of pyroracemic acid on boiling with barium hydroxide solution into uvitic acid, $C_6H_3[1,3,5](CH_3)(CO_2H)_2$ (Vol. II), and uvic acid or pyrotritaric acid (Vol. II), is noteworthy. The first step is the separation of oxalic acid with the formation of methyl dihydrotrimesic acid; then, CO_2 is given off and dihydrouvitic acid results; finally, oxidation produces uvitic acid (Ann. **305,** 125). These intermediate compounds can be avoided by condensing pyroracemic acid with acetaldehyde, a reaction which is of general application. For the condensation of pyroracemic acid with formaldehyde, see tetramethylene dioxalic acid (Vol. II).

On standing, a slow aldol-like condensation takes place, which can be accelerated by the presence of hydrochloric acid, whereby two molecules of pyroracemic acid unite to form α-ketovalerolactone-γ-carboxylic acid,



$$\begin{array}{ll} COOH{\cdot}C(CH_3) & —O \\ | & \quad | \\ CH_2{\cdot}CO{\cdot} & CO \end{array}$$

(*q.v.*). Heated with hydrochloric acid this substance gives up CO_2, and pyrotartaric acid is formed (see also C. 1904, II. 1453). The salts of pyroracemic acid are caused to undergo polymerization by the action of alkalis to salts of *para*-pyroracemic acid and *meta*-pyroracemic acid (Ann. **317,** 1 : **319,** 121 : C. 1901, II. 1262 : 1903, I. 16).

Pyroracemic ethyl ester, b.p. 146° ; *acetal,* $CH_3C(OC_2H_5)_2{\cdot}CO_2C_2H_5$, b.p. 190° (see also α-ethoxy acrylic ester, p. 452).

Halogen Substitution Products of Pyroracemic Acid.—*Trichloropyroracemic acid,* $CCl_3{\cdot}CO{\cdot}CO_2H + H_2O = CCl_3{\cdot}C(OH)_2COOH$, m.p. 102°, is produced (1) when $KClO_3$ and HCl act on gallic acid and salicylic acid ; (2) by the action of chlorine water on chlorofumaric acid (Ber. **26,** 656) ; (3) from trichloroacetyl cyanide.

Substitution products result by heating the acid with bromine and water to 100°. *Dibromopyruvic acid,* $CBr_2HC(OH)_2CO_2H + H_2O$, m.p. 89° (anhydrous). *Tribromopyruvic acid,* $CBr_3C(OH)_2{\cdot}CO_2H + H_2O$, m.p. 90° (anhydrous). Heated with water or ammonia it breaks up into bromoform, $CHBr_3$, and oxalic acid.

Homologues of Pyroracemic Acid.

Propionylformic acid, $CH_3CH_2CO{\cdot}COOH$, b.p. 74–78°/25 mm., is also obtained by the transformation of vinylglycollic acid (p. 452) ; *ethyl ester,* b.p. 162° (C. 1904, II. 1706). *Butyrylformic acid,* $CH_3CH_2CH_2CO{\cdot}CO_2H$, b.p. 115°/83 mm. ; *ethyl ester,* b.p. 72–77°/10 mm., is produced from α-oximinovaleric ester (mode of formation No. 2, p. 462). *Dimethylpyroracemic acid,* $(CH_3)_2CHCO{\cdot}COOH$, m.p. 31°, b.p. 66°/10 mm., is produced by the cleaving action of hydrochloric acid on aminodimethylacrylic acid (p. 454) (C. 1902, I. 251). *Trimethylpyroracemic acid,* $(CH_3)_3C{\cdot}CO{\cdot}COOH$, m.p. 90°, b.p. 185°, results when pinacolin is oxidized with $KMnO_4$ (Ber. **23,** R. 21 : C. 1898, I. 202). iso*Butylpyroracemic acid,* $(CH_3)_2CHCH_2{\cdot}CH_2CO{\cdot}COOH$, m.p. 22°, is obtained from *iso*butylcitraconic acid and *iso*butylmesaconic acid (Ann. **305,** 60) ; *ethyl ester,* b.p. 74°/11 mm., is prepared from α-oximino*iso*caproic ester (C. 1904, II. 1737 : 1906, II. 1824).

Nitrogen Derivatives of the α-Ketonic Acids

(1) **Acyl cyanides, α-ketone nitriles** result on heating acid chlorides or bromides with silver cyanide :

$$C_2H_3O{\cdot}Cl + AgNC = C_2H_3O{\cdot}CN + AgCl ;$$

and when the aldoximes of the α-aldehyde ketones are treated with dehydrating agents, such as acetic anhydride (p. 406) (Ber. **20,** 2196) :

$$CH_3{\cdot}CO{\cdot}CH : NOH = CH_3{\cdot}CO{\cdot}CN + H_2O.$$

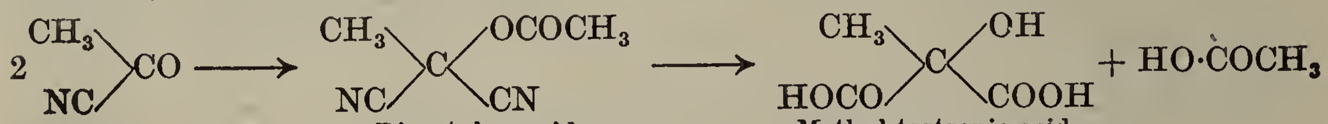
The acid cyanides are not very stable, and, unlike the alkyl cyanides, are converted by water or alkalis into the *fatty acid* and hydrogen cyanide,

$$CH_3CO{\cdot}CN + H_2O = CH_3CO{\cdot}OH + HNC.$$

With concentrated hydrochloric acid, on the contrary, they undergo a transposition similar to that of the alkyl cyanides (p. 324), in which water is absorbed, and the amides of the α-*ketonic acids* are intermediate products (Claisen) :

$$CH_3COCN \xrightarrow{H_2O} CH_3COCONH_2 \xrightarrow[HCl]{H_2O} CH_3COCOOH + NH_4Cl.$$

Acetyl cyanide, *pyruvic nitrile,* $CH_3CO{\cdot}CN$, b.p. 93°. When preserved for some time, or by the action of KOH or sodium, it is transformed into *diacetyl cyanide,* $C_6H_6O_2N_2$, m.p. 69°, b.p. 208°, which can also be prepared from acetic anhydride, potassium cyanide and hydrochloric acid in ether at 0°. Hydrolysis converts it into methyl tartronic acid, probably according to the following scheme (Monatsh. **15,** 773) :



Diacetyl cyanide. Methyl tartronic acid.

Propionyl cyanide, CH_3CH_2COCN, b.p. 108–110°. *Dipropionyl cyanide*, $(C_3H_5OCN)_2$, m.p. 59°, and b.p. 200–210°, behaves like diacetyl cyanide (Ber. **26**, R. 372).

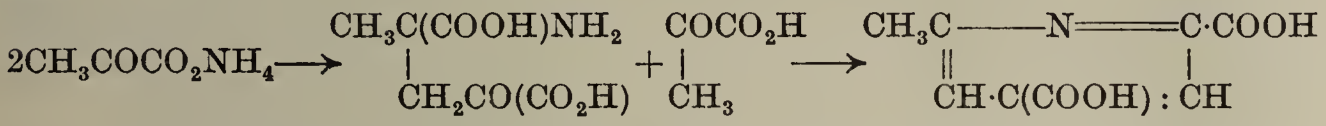
Butyryl cyanide, C_3H_7COCN, b.p. 133–137°, and iso*butyryl cyanide*, C_3H_7COCN, b.p. 118–120°, polymerize readily to dicyanides, which pass into alkyl tartronic acids on treatment with hydrochloric acid.

Pyroracemic amide, $CH_3CO{\cdot}CONH_2$, m.p. 124° ; *propionylformamide*, $C_2H_5{\cdot}CO{\cdot}CONH_2$, m.p. 116°, are produced from α-ketone nitriles and concentrated hydrochloric acid (Ber. **13**, 2121).

Pyruvyl ethyl imidochloride, $CH_3COCCl : NC_2H_5$, is a yellowish oil produced by the union of acetyl chloride with ethyl *iso*cyanide (Ann. **289**, 298).

*Pyruvyl hydroximic chloride, chloro*iso*nitrosoacetone*, $CH_3COC(NOH)Cl$, m.p. 105°, is formed by the action of nitric acid on chloroacetone ; or by the action of chlorine on *iso*nitrosoacetone ; or by the action of hydrochloric acid on *acetyl methyl nitrolic acid*, $CH_3{\cdot}CO{\cdot}C(=NOH)NO_2$—the product resulting from the action of nitric acid on acetone (Ann. **309**, 241). The *oxime*, $CH_3{\cdot}C : NOH{\cdot}C(: NOH)O{\cdot}NO$, m.p. 97° (decomp.).

(2) *Behaviour of Ammonia and Aniline with Pyroracemic Acid.*—The ammonium salt, like the other alkali salts, undergoes condensation in neutral or alkaline solution. At first an amino-ketone dicarboxylic acid is formed, which loses formic acid and passes into uvitonic acid, a picoline dicarboxylic acid (C. 1904, II. 192) :



$$2CH_3COCO_2NH_4 \longrightarrow \begin{array}{l}CH_3C(COOH)NH_2\\ \quad |\\ \quad CH_2CO(CO_2H)\end{array} + \begin{array}{l}COCO_2H\\ |\\ CH_3\end{array} \longrightarrow \begin{array}{l}CH_3C\text{——}N{=\!=\!=}C{\cdot}COOH\\ \quad \| \qquad\qquad\qquad\quad |\\ CH{\cdot}C(COOH) : CH\end{array}$$

Aniline and pyroracemic acid produce *pyruvic acid anil*, $C_6H_5N : C(CH_3)COOH$-m.p. 126° (decomp.), which undergoes a similar condensation with a further molecule of pyroracemic acid to form α-methyl cinchonic acid, aniluvitonic acid (Vol. III).

In acid solution one molecule of NH_3 and two of pyroracemic acid unite to form iminodilactic acid (*cf.* Thiodilactic acid, p. 430), with the probable formation of intermediate compounds. On losing CO_2 it forms *N*-acetylalanine (C. 1904, II. 193) :

$$CH_3C(COOH)(OH)NHC(OH)(CH_3)COOH \xrightarrow[-\,H_2O]{-\,CO_2} CH_3CONH{\cdot}CH(CH_3)CO_2H.$$

(3) α-**Oximino-fatty acids** or *oximes* of the α-*ketone acids* are formed (*a*) by the action of NH_2OH on α-ketone acids ; (*b*) by the interaction of mono-alkyl acetoacetic acids and nitrous acid, alkyl nitrites, nitrosyl sulphuric acid or nitrosyl chloride (Ber. **11**, 693; **15**, 1527 : C. 1904, II. 1457, 1706) :

$$CH_3COCH(CH_3)CO_2R + HO_3SONO \longrightarrow CH_3CO_2SO_3H + HON : C(CH_3)CO_2R.$$

Further action of nitrous acid converts the α-oximino-esters into α-ketone esters (p. 462). Acetic anhydride causes the splitting off of water and CO_2 with formation of acid nitriles.

α-**Oximinopropionic acid**, iso*nitrosopropionic acid*, $CH_3C(: NOH){\cdot}CO_2H$, decomposes at 177° ; *methyl ester*, m.p. 69°, b.p. 123°/14 mm. ; *ethyl ester*, $CH_3C=(NOH)CO_2C_2H_5$, m.p. 94°, b.p. 238° (Ber. **27**, R. 470) ; *amide*, $CH_3{\cdot}C(: NOH){\cdot}CONH_2$, m.p. 174° (Ber. **28**, R. 766 ; C. 1904, II. 1457). α-**Oximinobutyric acid**, $CH_3{\cdot}CH_2C(=NOH)CO_2H$. α-Oximidovalerianic acid, and a number of other homologues and their esters have also been prepared. α-Oximido-dibromopyroracemic acid has been obtained in two modifications (Ber. **25**, 904).

(4) *Pyruvic ester hydrazone*, $NH_2{\cdot}N : CMe{\cdot}COOEt$, m.p. 116° (J. pr. Chem. [2] **44**, 554 : Helv. Chim. Acta. **4**, 231) results from pyroracemic acid and hydrazine. Mercuric oxide converts its methyl ester into α-diazopropionic methyl ester.

(5) α-*Diazopropionic ester*, $CH_3{\cdot}C(N_2){\cdot}CO_2Et$, b.p. 65–68°/41 mm., is obtained from the hydrochloride of alanine ethyl ester by the action of KNO_2. It is a yellow oil, which is partially decomposed, by distillation at ordinary pressure, into dimethyl fumaric ethyl ester. α-*Diazobutyric ester*, b.p. 63–65°/11 mm., and α-*diazo*iso*caproic ester*, b.p. 70–73°/12 mm., both resemble diazoacetic ester (p. 458) in their behaviour, but are more easily decomposed, and are therefore more difficult to obtain pure (Ber. **37**, 1261).

(6) *Pyroracemic acid, phenylhydrazone*, $CH_3C(=NNHC_6H_5)CO_2H$, m.p. about 192° (decomp.), is not only formed by the action of phenylhydrazine on pyroracemic acid (Ber. **21**, 984), but also by hydrolysis of the reaction-product from diazobenzene chloride and methyl acetoacetic ester (Ber. **20**, 2942, 3398 : **21**, 15 : Ann. **278**, 285 : C. 1901, II. 212).

Pyroracemic *ethyl ester* yields two isomers with phenylhydrazine, which are separable by chloroform : *phenylhydrazones*, m.p. 32° and 119° (C. 1900, II. 1150).

(7) *Semicarbazones* of the α-ketonic acids, $NH_2CO{\cdot}NHN:CRCO_2H$, and their esters, see C. 1904, II. 1706, etc.

II. β-Ketonic Acids

In the β-ketonic acids the ketone oxygen atom is attached to the second carbon atom, counting from the carboxyl group. These compounds are very unstable either in the free state or as salts. Heat decomposes them into carbon dioxide and ketones. The CO and CO_2H groups are attached to the same carbon atom, and, in this respect, the compounds resemble malonic acid and its mono- and di-substitution products (see later), in which two carboxylic groups are attached to the same carbon atom ; these also give off CO_2 when heated. Their esters, on the other hand, are stable, can be distilled without decomposition, and serve for innumerable syntheses.

Acetoacetic acid, *acetonecarboxylic acid*, *β-ketobutyric acid* [3-butanone acid], $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO_2H$. To obtain the acid, the esters are hydrolysed in the cold by dilute potassium hydroxide solution (the rate of hydrolysis is independent of the concentration : Ber. **32**, 3390 : **33**, 1140) ; the acid is liberated with sulphuric acid, and the solution shaken with ether (Ber. **15**, 1781 : **16**, 830). Concentrated over sulphuric acid, acetoacetic acid is a thick liquid, strongly acid, and miscible with water. When heated, it yields carbon dioxide and acetone :

$$CH_3CO{\cdot}CH_2CO_2H = CH_3CO{\cdot}CH_3 + CO_2.$$

Nitrous acid converts it at once into CO_2 and *iso*nitrosoacetone (p. 407). Its salts are not very stable ; it is difficult to obtain them pure, since they undergo changes similar to those of the acid. Ferric chloride imparts to them, and also to the esters, a violet-red coloration. The sodium salt is found in urine in certain pathological conditions, particularly in diabetic coma.

The *homologous β-Ketone acids* can also be prepared by the hydrolysis of their esters with hot concentrated sulphuric acid : the resulting liquid may contain the sulphates of the *enol* forms : $RC(OSO_3H){\cdot}CHCO_2H$. The free acids, like acetoacetic acid itself, easily decompose into CO_2 and ketones (C. 1904, II. 1707).

The stable acetoacetic esters, $CH_3CO{\cdot}CH_2CO_2R$, are produced as sodium derivatives by the action of metallic sodium on acetic esters.

The free esters result upon treating their sodium compounds with acids, and are obtained pure by distillation.

The acetoacetic esters are liquids, which dissolve with difficulty in water, and possess an ethereal odour. They can be distilled without decomposition.

The esters of acetoacetic acid, contrary to expectation, possess an acid-like character. They dissolve in alkalis, forming salt-like compounds in which a hydrogen atom is replaced by metals.

History.—Geuther in 1863 investigated the action of sodium on acetic ester. According to the theory at that time current, acetic acid should contain two hydrogen atoms replaceable by metals, the one easily replaced, the other with difficulty. Geuther attempted to form the disodium derivative by heating sodium acetate with metallic sodium and when that failed, attempted to obtain the ester-salt, $CH_2 : CH(OEt)(ONa)$ (present-day formula), by the action of sodium on ethyl acetate. Instead of this he obtained a *compound*, $C_6H_9O_3Na$, which on decomposition by acid formed a *compound*, $C_6H_{10}O_3$, which possessed acidic and ester properties, and which he named ethyldiacetic acid. Simultaneously, and independently of Geuther, Frankland and Duppa investigated the action of sodium and alkyl iodides on acetic ester, as a sequel to their work on the action of zinc and alkyl iodides on oxalic ester. Wislicenus, Claisen, A. Michael and Scheibler have done much to explain the mechanism of the reaction.

The difficulty of the problem lay largely in the fact that in many of its reactions, such as the formation of an acetal with orthoformic ester, the formation of acetone on hydrolysis, acetoacetic ester behaves as if it has a *ketonic* structure (I), which is also supported by many of its physical properties. On the other hand, many of its reactions, its acid character (solubility in alkalis), its colour reaction with ferric chloride, its unsaturated character (addition of bromine) and the formation of an *O*-derivative by the action of chloroformic ester, are better in accord with the " *enolic* " formula (II):

β-Ketobutyric ester . .	$CH_3{\cdot}CO{\cdot}CH_2{\cdot}COOEt$	(I)
β-Hydroxycrotonic ester .	$CH_3{\cdot}C(OH) : CH{\cdot}COOEt$	(II)

It is found that liquid or dissolved acetoacetic ester is an equilibrium mixture of the two forms, the position of equilibrium depending on the temperature and the nature of the solvent. If an alkali acts on this equilibrium mixture, that *enol*-form already present is attacked, and to maintain the equilibrium more of the *keto*-form must change to the *enol*-, which is removed as fast as it is formed, so that eventually the whole amount is dissolved. In this reaction, therefore, the mixture behaves as 100% enol, and similarly, by the action of ketone reagents, the keto-form is removed from the equilibrium, and the enol-form initially present changes to the keto-form, the mixture then behaving as a pure ketonic compound. Acetoacetic ester forms the classical example of that form of dynamic isomerism known as keto-enol tautomerism.

Formation of Acetoacetic Ester and its Homologues

(1) *The " Ester-condensation " in General*

As already stated, acetoacetic ester is obtained in the form of its sodium derivative by the action of sodium ethoxide, sodium or sodamide on acetic ester:

(*a*) $2CH_3{\cdot}COOC_2H_5 + NaOC_2H_5 \longrightarrow CH_3{\cdot}C(ONa) : CH{\cdot}COOC_2H_5 + C_2H_5OH.$

(*b*) $2CH_3{\cdot}COOC_2H_5 + 2Na \longrightarrow CH_3{\cdot}C(ONa) : CH{\cdot}COOC_2H_5 + H_2.$

(*c*) $2CH_3{\cdot}COOC_2H_5 + 2NaNH_2 \longrightarrow CH_3{\cdot}C(ONa) : CH{\cdot}COOC_2H_5 + C_2H_5ONa + 2NH_3.$

The reaction (*a*) is inhibited by the alcohol formed, whereas this does not occur in (*b*) and (*c*) where the alcohol is converted into alcoholate by the excess of reagent. The reaction (*b*) is to some extent influenced by the reducing action of the hydrogen evolved.

At the conclusion of the reaction, the ester is liberated from its sodium derivative by the use of acid.

The formation of acetoacetic ester in this way is a special case of a very general reaction, whereby the carbethoxy group of any ester (A) enters into reaction with the methyl or methylene group of a second compound (B) which is activated by the immediate proximity of a carbonyl group:

$$\underset{(A)}{R\cdot CO\cdot OEt} + \underset{(B)}{CH_2R\cdot CO\cdot} \longrightarrow R\cdot CO\cdot CHR'\cdot CO\cdot + EtOH.$$

(A) must always be an ester. (B) can be either an ester, identical with or different from (A), or a ketone, the latter reaction being a valuable method for the preparation of 1 : 3-diketones. (Mixed ester condensation, *Wislicenus*, Ber. **19**, 3225: *Claisen*, Ber. **20**, 651: Ester-ketone condensation, *Claisen*, Ber. **20**, 655), *e.g.*:

$$CH_3\cdot COOEt + Na + CH_3\cdot CO\cdot CH_3 \longrightarrow \underset{\text{Sodium derivative of acetylacetone.}}{CH_3\cdot C(ONa) : CH\cdot CO\cdot CH_3.}$$

The mechanism of the ester condensation, like the formula of acetoacetic ester, has been the objective of many investigations over the last fifty years, and is not yet entirely settled. The original conception, that *C*-metallic derivatives such as $CH_2Na\cdot COOEt$ are involved, has now been entirely abandoned. It has been shown that many ester condensations will take place with an alcoholic solution of sodium ethoxide, under conditions which preclude the possible formation of a *C*-sodium derivative. (Claisen, Ber. **20**, 2178, etc.) The mechanism is taken as involving the intermediate formation of *O*-sodium derivatives. Two of these have to be considered, (I) the addition product of sodium ethoxide and ethyl acetate, $CH_3\cdot C(OEt)_2\cdot ONa$ (Claisen, Ber. **20**, 651), and (II) the true *O*-sodium derivative, acetic ester sodium enolate, $CH_2 : C(OEt)\cdot ONa$ (*Michael*, *Claisen*, Ber. 38, 714: *Scheibler*, Ann. **458**, 1), which can be considered as arising from (I) by loss of alcohol, or directly from acetic ester and sodium ethoxide:

$$CH_3\cdot C\begin{smallmatrix}\diagup O\\ \diagdown OEt\end{smallmatrix} + NaOEt \longrightarrow CH_2 : C\begin{smallmatrix}\diagup ONa\\ \diagdown OEt\end{smallmatrix} + EtOH.$$

Each of these views leads to a fundamentally different view of the machanism of the ester condensation, in one the action of the sodium being on the carbethoxy component of the reaction, in the other, on the methyl component. The formation of benzoyl-acetic ester is thus represented either as from $C_6H_5\cdot C(OEt)_2ONa + CH_3\cdot COOEt$ or from $C_6H_5\cdot CO\cdot OEt + CH_2 : C(OEt)\cdot ONa$.

Claisen (Ber. **20**, 651) supports the first alternative, and gives the equation:

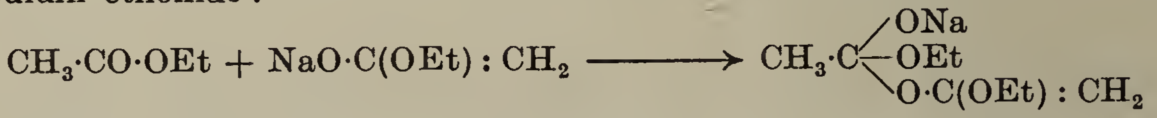
$$CH_3\cdot C(OEt)_2\cdot ONa + CH_3\cdot COOEt \longrightarrow CH_3\cdot C(ONa) : CH\cdot COOEt + 2EtOH.$$

Swarts (Bull. Soc. Chim. Belg. 35, 412) supports this conception by the fact that such an addition compound can actually be isolated from trifluoroacetic ester and sodium ethoxide, and this compound reacts with acetic ester to give a nearly quantitative yield of ethyl sodiotrifluoroacetoacetate:

$$CF_3\cdot C(OEt)_2\cdot ONa + CH_3\cdot COOEt \longrightarrow CF_3\cdot C(ONa) : CH\cdot COOEt + 2EtOH.$$

Claisen (Ber. **38**, 709) gives the following equations to show how the action may take place with the intermediate formation of (II):

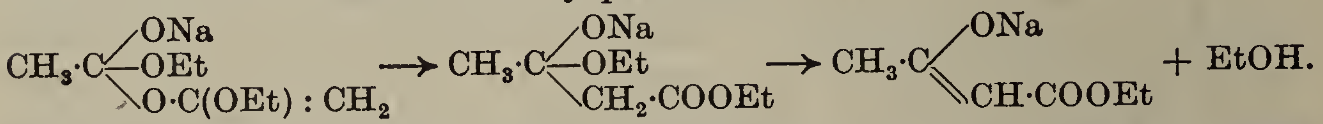
(*a*) Addition of the enolate to ethyl acetate, similarly to the addition of sodium ethoxide:



(III)

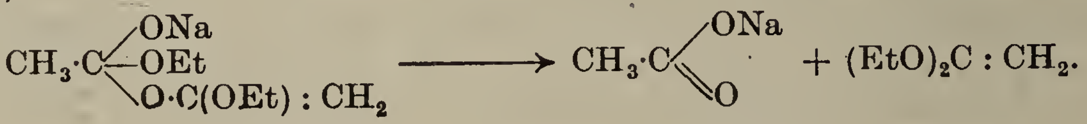
$$CH_3\cdot CO\cdot OEt + NaO\cdot C(OEt) : CH_2 \longrightarrow CH_3\cdot C\begin{smallmatrix}\diagup ONa\\ -OEt\\ \diagdown O\cdot C(OEt) : CH_2\end{smallmatrix} \qquad (III)$$

(*b*) The lower group in the compound (III) is then assumed to become detached, and subsequently reattached by means of the methylene group, a reaction for which there are many parallels:



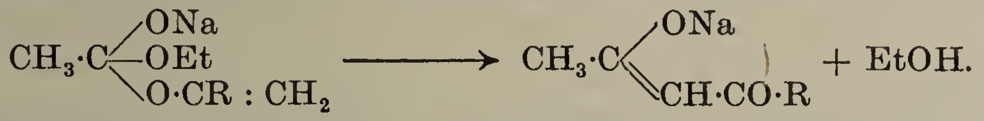
$$CH_3\cdot C\begin{smallmatrix}\diagup ONa\\ -OEt\\ \diagdown O\cdot C(OEt) : CH_2\end{smallmatrix} \longrightarrow CH_3\cdot C\begin{smallmatrix}\diagup ONa\\ -OEt\\ \diagdown CH_2\cdot COOEt\end{smallmatrix} \longrightarrow CH_3\cdot C\begin{smallmatrix}\diagup ONa\\ \\ \diagdown\!\!\diagdown CH\cdot COOEt\end{smallmatrix} + EtOH.$$

The formation of keten acetal, $CH_2 : C(OEt)_2$ as a by-product (*Scheibler* and *Ziegener*, Ber. **55**, 792) can also be explained by the intermediate formation of (III):



$$CH_3\cdot C\begin{smallmatrix}\diagup ONa\\ -OEt\\ \diagdown O\cdot C(OEt) : CH_2\end{smallmatrix} \longrightarrow CH_3\cdot C\begin{smallmatrix}\diagup ONa\\ \\ \diagdown\!\!\diagdown O\end{smallmatrix} + (EtO)_2C : CH_2.$$

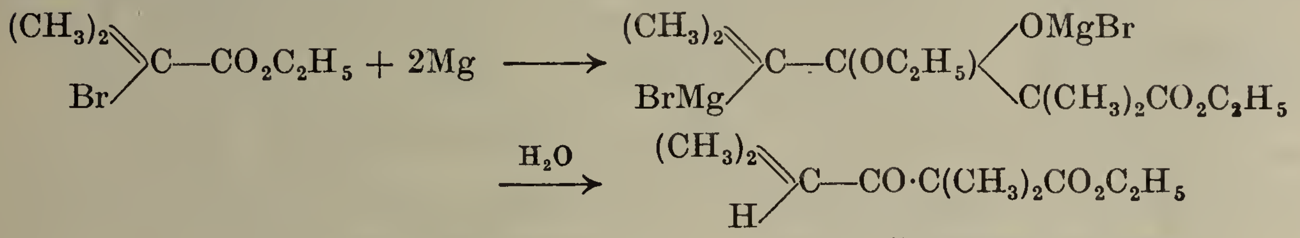
The mechanism of the ketone condensation is precisely similar, the only difference being the formation of the ketone enolate instead of the ester enolate



$$CH_3{\cdot}C\begin{cases}ONa\\OEt\\O{\cdot}CR:CH_2\end{cases} \longrightarrow CH_3{\cdot}C\begin{cases}ONa\\CH{\cdot}CO{\cdot}R\end{cases} + EtOH.$$

For a different formulation of the addition products postulated by Claisen as "molecular compounds," see Scheibler and Marhenkel (Ann. **458**, 4).

(2) A further general method for the synthesis of β-ketone-acid esters consists in the action of magnesium on α-bromo-fatty acid esters in ethereal solution (Ber. **41**, 589, 954):



$$\begin{matrix}(CH_3)_2\\Br\end{matrix}\!\!>C{-}CO_2C_2H_5 + 2Mg \longrightarrow \begin{matrix}(CH_3)_2\\BrMg\end{matrix}\!\!>C{-}C(OC_2H_5)\begin{cases}OMgBr\\C(CH_3)_2CO_2C_2H_5\end{cases}$$

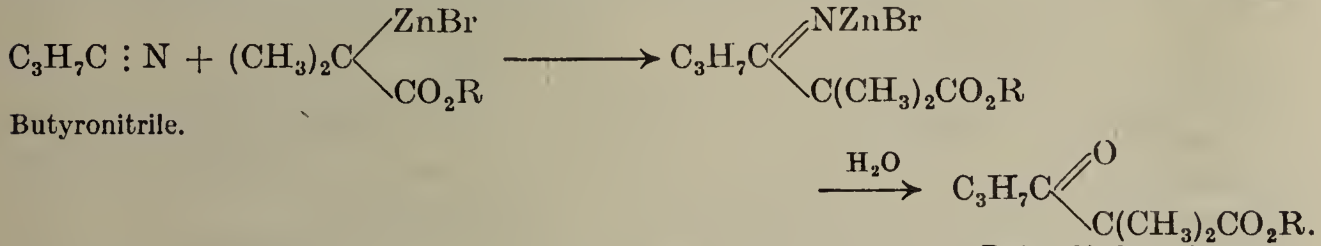
$$\xrightarrow{H_2O} \begin{matrix}(CH_3)_2\\H\end{matrix}\!\!>C{-}CO{\cdot}C(CH_3)_2CO_2C_2H_5$$

*iso*Butyryl*iso*butyric ester.

$$+ MgBr_2 + MgO + C_2H_5OH.$$

(3) A further synthesis depends on the action of metallo-organic compounds on nitriles:

(*a*) Acid nitriles are condensed with α-bromo-fatty esters by zinc, and the product is decomposed with water (C. 1901, I. 724):



$$C_3H_7C:N + (CH_3)_2C\begin{cases}ZnBr\\CO_2R\end{cases} \longrightarrow C_3H_7C\begin{cases}NZnBr\\C(CH_3)_2CO_2R\end{cases}$$

$$\xrightarrow{H_2O} C_3H_7C\begin{cases}O\\C(CH_3)_2CO_2R.\end{cases}$$

Butyronitrile.

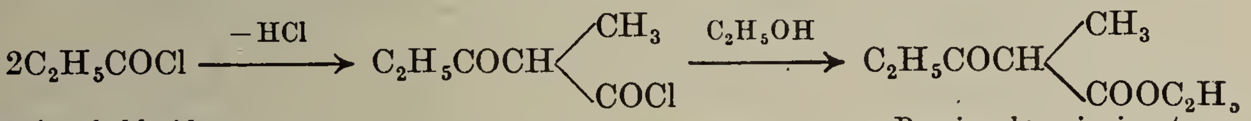
Butyryl*iso*butyric ester.

(*b*) The condensation of cyanoacetic ester with magnesium alkyl iodides and subsequent action of water also produces β-ketone-acid esters (C. 1901, I. 1195):

$$N:CCH_2CO_2R \xrightarrow{IMgC_2H_5} C_2H_5C(:NMgI)CH_2CO_2R \xrightarrow{H_2O} C_2H_5COCH_2CO_2R.$$

Cyanoacetic ester. Propionyl acetic ester.

(4) The higher esters can also be prepared by the action of ferric chloride on acid chlorides, whereby a ketonic acid chloride is first formed. Water causes the loss of CO_2, forming a ketone, but the action of alcohol is to produce the ketonic acid ester (Hamonet, Ber. **22**, R. 766):



$$2C_2H_5COCl \xrightarrow{-HCl} C_2H_5COCH\begin{cases}CH_3\\COCl\end{cases} \xrightarrow{C_2H_5OH} C_2H_5COCH\begin{cases}CH_3\\COOC_2H_5\end{cases}$$

Propionyl chloride. α-Propionylpropionic ester.

The higher chlorides, such as butyryl and œnanthylic, can be employed in this reaction.

(5) When α-acetylene carboxylic acids are boiled with alcoholic potassium hydroxide, water is taken up and β-acylacetic acids result. By esterification with alcohol and mineral acids at 0°, the β-ketonic acid esters are formed (C. 1903, I. 1018):

$$C_6H_{13}C{\equiv}C{\cdot}CO_2H \xrightarrow{H_2O} C_6H_{13}CO{\cdot}CH_2CO_2H \longrightarrow C_6H_{13}CO{\cdot}CH_2COOC_2H_5$$

Hexyl propiolic acid. Hepto-acetic ester.

(6) Finally, certain syntheses have been performed, in isolated cases, from aldehydes and diazoacetic ester (p. 458) (Ber. **40**, 3000):

$$CCl_3CHO + N_2CHCO_2C_2H_5 \longrightarrow CCl_3CO{\cdot}CH_2CO_2C_2H_5 + N_2.$$

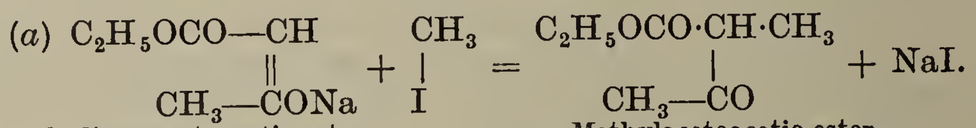
Reactions of Acetoacetic Ester.

Acetoacetic ester is a reagent of very wide applicability in the synthesis of organic compounds. The reasons of its great value are

(i) the ready introduction of substituents into the CH_2 group, (ii) the hydrolysis of the ester and its substitution products by the action of acids or alkalis with the formation of fatty acids and ketonic compounds.

(1) The interaction between the sodium compound of acetoacetic ester and alkyl halides, especially the iodides and bromides, results in the formation of homologous esters.

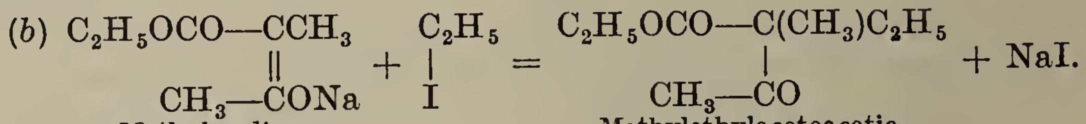
An examination of the structural formula for the acetoacetic ester reveals that only one hydrogen is replaceable by sodium. The metallic compound reacts with the halogen alkyl, whereby the sodium salt is formed and the alkyl group becomes attached to the α-C atom.



$$(a)\ \begin{array}{r}C_2H_5OCO—CH\\ \|\ \ \ \\ CH_3—CONa\end{array} + \begin{array}{c}CH_3\\ |\\ I\end{array} = \begin{array}{c}C_2H_5OCO\cdot CH\cdot CH_3\\ |\\ CH_3—CO\end{array} + NaI.$$

Sodium acetoacetic ester. α-Methylacetoacetic ester.

The mono-alkyl substituted ester can take up an atom of sodium and again react as above:



$$(b)\ \begin{array}{r}C_2H_5OCO—CCH_3\\ \|\ \ \ \\ CH_3—CONa\end{array} + \begin{array}{c}C_2H_5\\ |\\ I\end{array} = \begin{array}{c}C_2H_5OCO—C(CH_3)C_2H_5\\ |\\ CH_3—CO\end{array} + NaI.$$

α-Methyl sodium acetoacetic ester. Methylethylacetoacetic ester.

According to Michael (J. pr. Chem. [2] **37**, 486: **46**, 189) the reaction consists of an addition of the alkyl halide to the enol double linkage, followed by splitting off of sodium halide.

The dialkylacetoacetic esters are incapable of enolization and do not form sodium derivatives.

By the action of acid chlorides, R·COCl, on the sodium derivative an exactly similar reaction takes place, with the formation of *C*-acyl derivatives. In the presence of pyridine, the action of acid chlorides or chloroformic esters on acetoacetic ester leads to the formation of *O*-acyl derivatives of the enol form (*cf.* p. 474). The two reactions are contrasted below:

$$CH_3\cdot C(ONa) : CH\cdot COOEt + CH_3\cdot COCl \longrightarrow CH_3\cdot CO\cdot CH(COCH_3)\cdot COOEt + NaC.$$

$$CH_3\cdot C(OH) : CH\cdot COOEt + CH_3\cdot COCl \xrightarrow{\text{Pyridine}} CH_3\cdot C(O\cdot COCH_3) : CH\cdot COOEt + \text{pyridine}, HCl.$$

A general prophecy as to whether a *C*- or an *O*-alkyl compound is obtained in any particular alkylation cannot at present be made, but comparing Claisen's results (Ann. **442**, 210) on the action of allyl bromide on phenol, acetoacetic ester and other dicarbonyl compounds, it is seen that the nature of the product depends very largely on

(*a*) The additive capacity of the double linkage.
(*b*) The mobility of the halogen in the alkyl halide employed.
(*c*) The nature of the solvent.

In broad terms it may be said that the greater (*a*) and (*b*) are, and the use of less dissociating solvents (*e.g.* benzene) lead to the formation of *C*-alkyl derivatives.

(2) Acetoacetic ester and its mono- and di-alkyl derivatives can be decomposed in two ways to form simpler compounds.

(*a*) By hydrolysis with dilute mineral acids or very dilute alkalis the products are a ketone, carbon dioxide and alcohol (*ketone decomposition*):

$$\begin{array}{l:l:l} CH_3{\cdot}CO{\cdot}CH_2{\cdot} & COO & C_2H_5 \\ \quad + \quad H & & OH \end{array} = \underset{\text{Acetone.}}{CH_3{\cdot}CO{\cdot}CH_3} + CO_2 + C_2H_5OH.$$

(*b*) By hydrolysis with concentrated alcoholic alkalis, the products are two molecules of fatty acid (or its salt) and alcohol (*acid decomposition*):

$$\begin{array}{l:l:l} CH_3{\cdot}CO{\cdot} & CH_2{\cdot}COO & C_2H_5 \\ \quad HO & H \qquad\quad H & OH \end{array} = \underset{\text{Acetic acid.}}{CH_3{\cdot}COOH} + CH_3COOH + C_2H_5OH.$$

The substituted acetoacetic esters are similarly decomposed, the ester $CH_3{\cdot}CO{\cdot}CRR'{\cdot}COOC_2H_5$ yielding the ketone $CH_3{\cdot}CO{\cdot}CHRR'$ when submitted to the ketone decomposition and the acids $CH_3{\cdot}COOH$ and $CHRR'{\cdot}COOH$ by the acid decomposition. (For ketone decomposition, see C. 1927, II. 2743.)

By means of the "acid decomposition" the higher acylacetic esters can be prepared, by converting ethyl acetoacetate into the *C*-acyl derivative and treating the product cautiously with alkali. The acetyl group is thereby preferentially split off (C. 1902, II. 1410), *e.g.*:

$$\underset{C\text{-butyrylacetoacetic ester.}}{C_3H_7{\cdot}CO{\cdot}CH(CO{\cdot}CH_3){\cdot}COOEt} \xrightarrow{NaOH} \underset{\text{Butyrylacetic ester.}}{C_3H_7{\cdot}CO{\cdot}CH_2{\cdot}COOEt} + CH_3{\cdot}COONa.$$

(*c*) The decomposition of mono- and di-alkyl-acetoacetic esters into mono- and di-alkylacetic esters can be carried out directly and completely by boiling with sodium ethoxide solution (*ester decomposition*) (Ber. **33**, 2670: **41**, 1260):

$$CH_3CO{\cdot}C(CH_3)_2CO_2R + ROH = CH_3CO_2R + (CH_3)_2CHCO_2R.$$

(3) The acetoacetic esters are converted by nascent hydrogen (sodium amalgam) into the corresponding β-hydroxy-acids (p. 421):

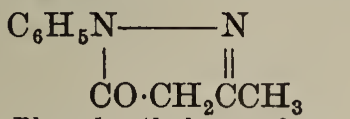
$$CH_3CO{\cdot}CH_2CO_2C_2H_5 + H_2 + H_2O = CH_3CH(OH){\cdot}CH_2CO_2H + C_2H_5OH.$$

(4) Chlorine and bromine produce halogen substitution products of the acetoacetic esters, the hydrogen of the —CH_2— group being replaced first.

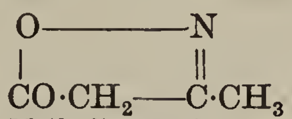
(5) PCl_5 replaces the oxygen of the β-CO group by 2 atoms of chlorine. The chloride, $CH_3CCl_2{\cdot}CH_2COCl$, readily loses hydrochloric acid and yields two chlorocrotonic acids (p. 344).

(6) Orthoformic ester replaces the oxygen of the β-CO group by two ethoxy-groups producing β-diethoxybutyric ester, which readily splits off alcohol and yields β-ethoxycrotonic ester (p. 453). This is a method of preparing *O*-alkyl derivatives.

(7) Ammonia, aniline, hydrazine and phenylhydrazine acting on acetoacetic ester produce the imine, anilide, hydrazone and phenylhydrazone, which can also be looked on as being respectively β-amino-, β-anilino-, β-hydrazino-, and β-phenylhydrazino-crotonic esters. Acetoacetic ester forms a semicarbazone with semicarbazide, and an oxime with hydroxylamine (Ber. **28**, 2731). The hydrazones and oximes of the β-ketonic esters easily give up alcohol and become converted into cyclic derivatives—*lactazams* and *lactazones* (*cf.* p. 461), usually known as pyrazolones and isoxazoles:



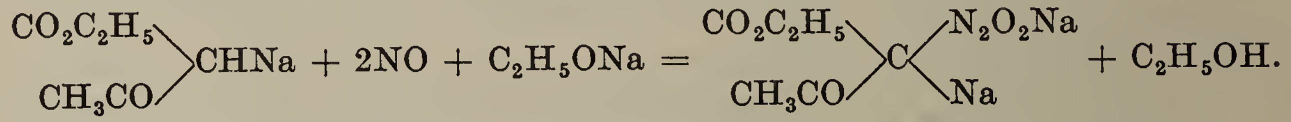
Phenylmethylpyrazolone.



Methylisoxazole.

One molecule of hydrazine converts acetoacetic ester into the *azine*, $(C_6H_{10}O_2):N—N:(C_6H_{10}O_2)$, m.p. 48°, which an excess of hydrazine easily transforms into two molecules of methylpyrazolone (Ber. **37**, 2820: **38**, 3036).

(8) Nitric oxide and sodium ethoxide change sodium acetoacetic ester into the disodium derivative of *iso*nitraminoacetoacetic ester (Ann. **300**, 89):

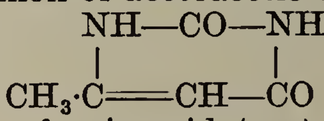


$$\begin{matrix}CO_2C_2H_5\\CH_3CO\end{matrix}\!\!>\!CHNa + 2NO + C_2H_5ONa = \begin{matrix}CO_2C_2H_5\\CH_3CO\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}N_2O_2Na\\Na\end{matrix} + C_2H_5OH.$$

(9) Nitrous acid changes the non-alkylated acetoacetic ester to the *iso*nitroso-derivatives, $CH_3CO{\cdot}C(:N{\cdot}OH)CO_2R$, which readily break up into *iso*nitroso-acetone, CO_2 and alcohols (see below). Nitrous acid, acting on monoalkyl acetoacetic esters, displaces the acetyl group and leads to the formation of α-*iso*nitroso-fatty acids (p. 460), whereas the free monoalkyl acetoacetic esters, under like treatment, split off CO_2 and yield *iso*nitroso-ketones (p. 406).

(10) Benzenediazonium chloride reacts with the *enol*-form of acetoacetic ester with the formation of the phenylhydrazone of pyruvic aldehyde (Ber. **21**, 549: Ann. **247**, 217). Intermediate stages of the reaction, see *Dimroth*, Ber. **40**, 2404, 4460: **41**, 4012.

(11) Diazomethane converts acetoacetic ester into β-methoxy-crotonic ester (p. 474) (Ber. **28**, 1626).

(12) An important reaction is the union of acetoacetic ester with urea, when water is eliminated and methyluracil,  $\begin{array}{l}NH{-}CO{-}NH\\ \vert \qquad\quad \vert\\ CH_3{\cdot}C{=}CH{-}CO\end{array}$, is formed. This is the parent substance in one synthesis of uric acid (*q.v.*).

(13) Amidines convert acetoacetic ester into pyrimidine compounds (Vol. III.).

(14) The action of sulphur chloride or thionyl chloride on acetoacetic ester is to produce thiodiacetoacetic ester, $S[CH(COCH_3)CO_2C_2H_5]_2$ (Ber. **39**, 3255).

Nucleus-synthetic Reactions.

(15) Heated alone, acetoacetic ester is changed to dehydracetic acid (*q.v.*), the δ-lactone of an unsaturated δ-hydroxy-diketone carboxylic acid.

(16) The action of sulphuric acid causes acetoacetic ester to pass into a condensation product, *iso*dehydracetic acid, the δ-lactone of an unsaturated δ-hydroxy-dicarboxylic acid.

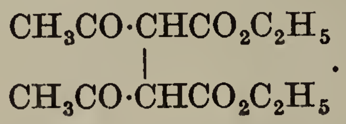
(17) Hydrocyanic acid unites with acetoacetic ester, forming the nitrile of α-methylmalic ester.

(18) (For the action of magnesium alkyl iodides on acetoacetic ester, see C. 1902, I. 1197.)

The nucleus-synthetic reactions of the *sodium derivative* of acetoacetic ester and copper acetoacetic ester are far more numerous.

(19) It has been repeatedly mentioned that the sodium acetoacetic esters could be applied in the building-up of the mono- and di-alkyl acetoacetic esters, and also, therefore, in the preparation of mono- and di-alkyl acetones, as well as mono- and di-alkyl acetic acids.

(20) Iodine converts sodioacetoacetic ester into diacetosuccinic ester:



$$\begin{array}{l}CH_3CO{\cdot}CHCO_2C_2H_5\\ \qquad\quad\ \vert\\ CH_3CO{\cdot}CHCO_2C_2H_5\end{array}.$$

This body is also produced in the electrolysis of sodioacetoacetic ester (Ber. **28**, R. 452).

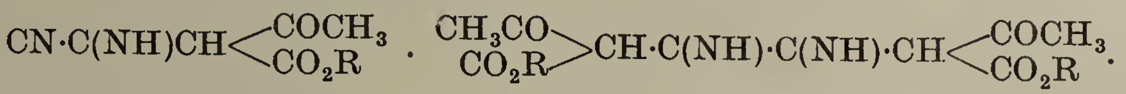
(21) Chloroform and sodioacetoacetic ester unite to form hydroxyuvitic acid, $C_6H_2(CH_3)(OH)(CO_2H)_2$.

(22) Other halogen compounds such as monochloroacetone, cyanogen chloride, acid halides, and monohalogen substitution products of mono- and di-carboxylic esters react with sodium acetoacetic ester. *Copper acetoacetic ester* is most advantageously used with phosgene (Ber. **19**, 19). (For greater detail see below.)

(23) Aldehydes, *e.g.* acetaldehyde, and acetoacetic ester unite to form ethylidenemono- and bis-acetoacetic esters. The latter γ-diketones especially are important, because by an intramolecular change, causing the loss of water from CO and CH_3, they condense to *cyclo*hexenone derivatives (Ann. **288**, 323), and with ammonia yield hydropyridine bodies. Acetone condenses with acetoacetic ester, forming *iso*propylideneacetoacetic ester (p. 481) (Ber. **30**, 481).

(24) Acetoacetic ester condenses similarly with orthoformic ester to the ethoxymethylene derivative $(C_6H_8O_2):CHOC_2H_5$, and to the methenyl derivative $(C_6H_8O_3):CH{\cdot}(C_6H_9O_3)$ (Ber. **26**, 2729).

(25) Cyanogen unites with sodioacetoacetic ester, forming the sodium compound of α-acetyl-β-cyano-β-iminopropionic ester, and of αα¹-diacetyl-ββ¹-di-imino-adipic ester (Ber. **35**, 4142):



$$\mathrm{CN{\cdot}C(NH)CH}<\begin{matrix}\mathrm{COCH_3}\\ \mathrm{CO_2R}\end{matrix} \quad . \quad \begin{matrix}\mathrm{CH_3CO}\\ \mathrm{CO_2R}\end{matrix}>\mathrm{CH{\cdot}C(NH){\cdot}C(NH){\cdot}CH}<\begin{matrix}\mathrm{COCH_3}\\ \mathrm{CO_2R}\end{matrix}.$$

(26) Phenols condense with acetoacetic ester to form coumarins (Vol. II) (Ber. **29**, 1794); quinones (Vol. II) form cumarones.

(27) Dihydrocollidinedicarboxylic ester is obtained smoothly by the interaction of aldehyde-ammonia and ethyl acetoacetate (Hantzsch's pyridine synthesis, Vol. III).

Methyl acetoacetate, b.p. 169°.

Ethyl acetoacetate. *Acetoacetic ester*, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}COOC_2H_5$, b.p. 181°/760 mm., b.p. 72°/12 mm., D_{20} 1·0256 is a colourless, mobile, pleasant-smelling liquid, slightly soluble in water and volatile in steam. Ferric chloride solution yields a violet colour, the reaction being due to the enol-form. It is broken down by acids with the formation of acetone, and by alkalis with the formation of acetic acid (see (2) above).

Liquid acetoacetic ester consists at room temperature of:

92·6% *Keto*-form, m.p. − 39°, b.p. 40–41°/2 mm., n_D^{10} 1·4225

7·4% *Enol*-form, liquid n_D^{10} 1·4480.

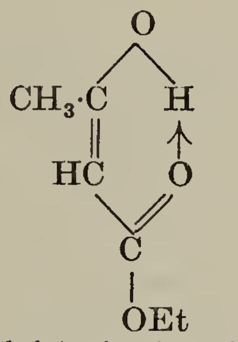
The separation of the keto and enol constituents of ethyl acetoacetate has been carried out by the following methods:

1. Freezing out of the pure keto-form at − 78° (Knorr, Ber. **44**, 1147).
2. The enol-form is obtained by the action of dry hydrogen chloride on ethyl sodioacetoacetate at − 78°.
3. By fractional distillation of the equilibrium mixture (Ber. **53**, 1410: **54**, 579: J.A.C.S. **50**, 3048).
4. By shaking out the keto-form with petroleum ether (Ann. **380**, 231).

It has been suggested (*Sidgwick*, J.C.S. **127**, 907) that the structure of the enol-form is more accurately represented by a "chelate-ring" structure, containing a co-ordinate linkage, than by the ordinary open-chain formula. This is based on the greater volatility of the enol- than the keto-form and the greater solubility in water of the keto-form (see p. 31):

$CH_3{\cdot}C(OH):CH{\cdot}COOEt$

Open-chain formula.



Chelate-ring formula.

At room temperature, the pure keto-form rapidly changes in part to the enol-form, with formation of the equilibrium mixture.

Quantitative estimation of enol-form, see p. 50: factors influencing the rate of attainment of equilibrium, see Bull. Soc. Chim. **35**, 762: rate of change of pure ester, see J.A.C.S. **50**, 3048.

Metallic derivatives.

The *sodium* derivative, $CH_3(CONa):CHCO_2C_2H_5$, crystallizes in long needles. *Copper* derivative $(C_6H_9O_3)_2Cu$, is produced when a copper acetate solution is shaken with an alcoholic solution of acetoacetic ester. When boiled with methyl alcohol, it undergoes alcoholysis, and is converted into $(C_6H_9O_3)CuOCH_3$ (Ber. **35**, 539); *aluminium* salt, m.p. 80°, b.p. 194°/8 mm. (C. 1900, I. 11).

The *thallium* derivative, m.p. 91–92°, is precipitated when thallous hydroxide solution is mixed with ethyl acetoacetate dissolved in alcohol. It is readily soluble in organic solvents (J.C.S. **127**, 2372).

Homologous β-Ketonic Esters.

Acid.	Formula.	B.p. of Ethyl Ester.	B.p. of Methyl Ester.
Methylacetoacetic .	$CH_3\cdot CO\cdot CHMe\cdot COOH$	187°	169°
Ethylacetoacetic . .	$CH_3\cdot CO\cdot CHEt\cdot COOH$	198°	190°
Dimethylacetoacetic .	$CH_3\cdot CO\cdot CMe_2\cdot COOH$	184°	—
Methylethylacetoacetic	$CH_3\cdot CO\cdot CMeEt\cdot COOH$	198°	—
Propylacetoacetic .	$CH_3\cdot CO\cdot CHPr\cdot COOH$	208°	—
Diethylacetoacetic .	$CH_3\cdot CO\cdot CEt_2\cdot COOH$	218°	—
Propionylacetic . .	$C_2H_5\cdot CO\cdot CH_2\cdot COOH$	92°/17 mm.	—
Butyrylacetic . . .	$C_3H_7\cdot CO\cdot CH_2\cdot COOH$	—	85°/14 mm.
Butyrylbutyric . .	$C_3H_7\cdot CO\cdot CHEt\cdot COOH$	223°	—
Butyryl*iso*butyric. .	$C_3H_7\cdot CO\cdot CMe_2\cdot COOH$	109°/29 mm.	—
*iso*Butyryl*iso*butyric .	$CHMe_2\cdot CO\cdot CMe_2\cdot COOH$	203°	—
Decoylacetic . . .	$C_9H_{19}\cdot CO\cdot CH_2\cdot COOH$	165°/13 mm.	—

Ethers and Thio-ethers of the β-Ketonic Acid Esters : *β-Diethoxybutyric ester* (*ortho-ethyl ether of acetoacetic ester*), $CH_3C(OC_2H_5)_2CH_2CO_2C_2H_5$, is obtained by the inter-reaction at low temperatures of acetoacetic and orthoformic esters under the influence of various reagents (*cf.* pp. 266, 290). It is an oil, which is converted by saponification into the crystallizable sodium salt of β-diethoxybutyric acid. This readily gives up CO_2, and yields into acetone ortho-ethyl ether (p. 266). The diethoxybutyric acid ester decomposes on distillation into alcohol and *β-ethoxycrotonic ester* (ethyl ether of *aci*-acetoacetic ester), $CH_3C(OC_2H_5):$-$CHCO_2C_2H_5$, m.p. 30°, b.p. 195°. This, on saponification, yields *β-ethoxycrotonic acid,* m.p. 137° ; it can also be formed from sodium ethoxide and β-chlorocrotonic acid (p. 344), and also from acetoacetic ester. On heating, it loses CO_2 and is converted into *iso*propenyl ethyl ether (p. 158) (Ann. **219**, 327 : **256**, 205). Alcoholic sodium ethoxide changes ethoxycrotonic ester back into di-ethoxybutyric ester (Ber. **29**, 1007). *β-Methoxycrotonic ester,* $CH_3C(OCH_3):CHCO_2C_2H_5$, m.p. 188°, is formed from acetoacetic ester and diazomethane (Ber. **28**, 1627).

A mixture of the two types of ethers—the ethyl ether of the *aci-* form and the ortho-ether of the keto- form of the β-ketonic esters—are obtained by boiling the homologous propiolic acid ester (p. 351) with alcoholic potassium hydroxide :

$$RC \vdots CCO_2C_2H_5 \longrightarrow RC(OC_2H_5):CHCO_2C_2H_5 \longleftrightarrow RC(OC_2H_5)_2\cdot CH_2CO_2C_2H_5.$$

Similarly, propiolic nitrile yields the ether of the ketonic acid nitrile (C. 1904, I. 659 : 1906, I. 912).

The *aci*-ether is readily hydrolysed by dilute sulphuric acid into the β-ketone acid ether.

ββ-Diethylthiolbutyric ester, $CH_3C(SC_2H_5)_2CH_2CO_2C_2H_5$, b.p. 138°/37 mm., is decomposed by hydrolysis into mercaptan and *β-ethylthiolcrotonic acid,* CH_3C-$(SC_2H_5):CHCO_2H$, m.p. 91° (Ber. **33**, 2801 : **34**, 2634).

Esters of the *aci*-β-Ketonic Acid Esters.

Acid chlorides and also halogen alkyls, acting on sodium acetoacetic ester, produce mainly the *C*-acyl compounds (described later among the diketo-carboxylic esters). Some *O*-acyl ester is also formed, which can be obtained as a main product, by the action of acid chlorides on acetoacetic ester in the presence of pyridine. The *O*-acyl esters are insoluble in alkalis, whilst the *C*-acyl esters are soluble, thus providing an easy method of separation. When heated with alkalis (potassium carbonate, sodium acetoacetic ester, etc.), the *O*-acyl esters are transformed into *C*-acyl esters. By heating to 240°, *O*-acetyl acetoacetic ester is converted to a small extent into di-acetoacetic ester (Ber. **38**, 546) :

$$CH_3C(OCOCH_3){=}CHCO_2C_2H_5 \longrightarrow CH_3CO{-}CH(COCH_3)CO_2C_2H_5.$$

Chlorocarbonic ester and sodium acetoacetic ester produce almost entirely β-carbethoxycrotonic ester, whilst with the copper salt acetylmalonic ester is formed (Ber. **37**, 3394). Both sodium and copper acetoacetic esters yield with phenyl *iso*cyanate acetylmalonanilic ester, $CH_3COCH(CONHC_6H_5)CO_2C_2H_5$ (Ber. **37**, 4627 : **38**, 22). It is therefore difficult to formulate a law for the acylation of these esters.

O-Acetylacetoacetic ester, β-acetoxycrotonic ester, $CH_3C(OCOCH_3) : CHCO_2C_2H_5$, b.p. 98°/12 mm. ; *methyl ester*, b.p. 95°/17 mm. *O-Butyryl acetoacetic methyl ester*, b.p. 105°/10 mm. *O-Propionylacetoacetic ethyl ester*, b.p. 106°/12 mm. (C. 1902, II. 1411). *O-Benzoyl ester*, m.p. 43°.

O-Carbethoxyacetoacetic ester, β-carbethoxyhydroxycrotonic ester, $CH_3C(OCO_2C_2H_5) : CHCO_2C_2H_5$, b.p. 131°/14 mm.

Nitrogen Derivatives of β-Ketone Carboxylic Acids

Amides.

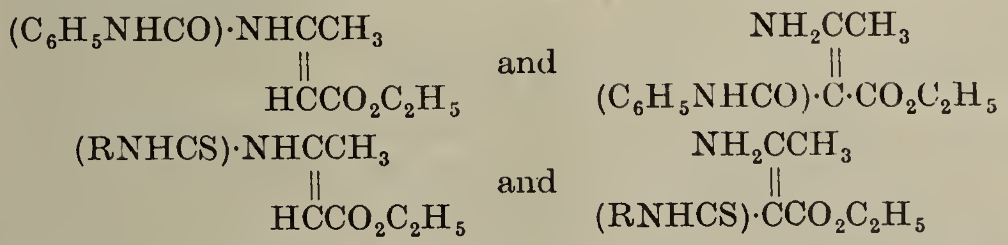
Aqueous ammonia acting on acetoacetic ester produces β-aminocrotonic ester (below), and *acetoacetic amide*, $CH_3COCH_2CONH_2$, m.p. 50°, which forms a crystalline copper salt (Ber. **35**, 583). *Methylacetoacetic amide*, $CH_3CO{\cdot}CH(CH_3){\cdot}CONH_2$, m.p. 73°, and *ethylacetoacetic amide*, m.p. 96°, are prepared respectively from methyl- and ethyl-acetoacetic esters and ammonia (Ann. **257**, 213). Similarly, *dimethyl* and *methylethyl-acetoacetic esters* form *amides*, m.p. 121° and 124° respectively ; di-ethyl acetoacetic ester does not form an amide (C. 1907, I. 401).

Nitriles.

Cyanoacetone : Acetoacetic acid nitrile, $CH_2CO{\cdot}CH_2CN$, b.p. 120–125°, is prepared from imino-acetoacetic nitrile (see below) and hydrochloric acid ; also by the transformation of α-methyl isoxazole (p. 407) (Ber. **25**, 1787). On heating it polymerizes suddenly. It cannot be obtained from chloroacetone and KCN. Chloroethyl methyl ketone and chloromethyl ethyl ketone do, however, react smoothly with potassium cyanide to form *α-methylacetoacetic nitrile*, $CH_3COCH(CH_3)CN$, b.p. 146° and *propionylacetonitrile*, $CH_3CH_2COCH_2CN$, b.p. 165° (C. 1900, I. 1123 : 1901, I. 96).

The reaction of aniline, hydrazine, phenylhydrazine and semicarbazide, hydroxylamine, nitrous acid, nitric oxide, diazomethane, benzene, diazo-salts, urea and the amidines, with β-keto-carboxylic esters are described on pp. 471, 472 (Nos. 7–13), in which the formation of pyrazolones from the β-keto-acid esters and the hydrazines is again to be remarked ; see phenyl methylpyrazolone and antipyrine (Vol. III).

β-Aminocrotonic ester, or *Imino-acetoacetic ester*, $CH_3C(NH_2) : CHCO_2C_2H_5$, or $CH_3C(NH)CH_2CO_2C_2H_5$, two modifications, m.pp. 20° and 33° (Ann. **314**, 202), is prepared from acetoacetic ester or β-chlorocrotonic ester (p. 344) and ammonia (Ber. **28**, R. 927). Aqueous hydrochloric acid converts it back into acetoacetic ester. Hydrochloric acid gas forms a salt which is decomposed by heat at 130° into ammonum chloride and δ-ole fine lactone carboxylic ester, *pseudo*-lutidostyril carboxylic ester (Ber. **20**, 445 : Ann. **236**, 292 : **259**, 172). NaClO and NaBrO produce chloro- and bromo-amino-crotonic esters, $CH_3C(NHX) : CHCO_2R$, which, on treatment with acids, lost NH_3, and are converted into α-chloro- and α-bromoacetoacetic ester (Ann. **318**, 371). On the action of nitrous acid, see Ber. **37**, 47. Phenyl *iso*cyanate and mustard oil combine with aminocrotonic ester, and form a mixture of *N*- and *C*- derivatives (Ann. **314**, 209 ; **344**, 19) :



$$\begin{array}{r} (C_6H_5NHCO){\cdot}NHCCH_3 \\ \| \\ HCCO_2C_2H_5 \end{array} \quad \text{and} \quad \begin{array}{c} NH_2CCH_3 \\ \| \\ (C_6H_5NHCO){\cdot}C{\cdot}CO_2C_2H_5 \end{array}$$

$$\begin{array}{r} (RNHCS){\cdot}NHCCH_3 \\ \| \\ HCCO_2C_2H_5 \end{array} \quad \text{and} \quad \begin{array}{c} NH_2CCH_3 \\ \| \\ (RNHCS){\cdot}CCO_2C_2H_5 \end{array}$$

β-Aminocrotonic acid nitrile, imino-acetoacetic nitrile, $CH_3C(NH_2) : CHCN$ or $CH_3C(NH){\cdot}CH_2CN$, m.p. 52°, results from the condensation of two molecules of acetonitrile by means of metallic sodium (J. pr. Chem. [2] **52**, 81).

Homologous β-alkylamino- and *β-di-alkylamino-acrylic esters*, $(C_2H_5)_2NCR : CCO_2C_2H_5$, and *nitriles*, $C_2H_5CH_2NHCR : CHCN$, are prepared by the addition of amines to the homologous propiolic esters and nitriles. Acids easily decompose them into the β-ketonic acid esters or nitriles, and amines (C. 1907, I. 25).

A *dinitrocaproic acid*, $CH_3C(NO_2)_2C(CH_3)_2CO_2H$, m.p. 215° with decomposition, is formed when camphor is boiled for a long time with nitric acid. It can be looked on as being a derivative of α-dimethyl acetoacetic acid (Ber. **26**, 3051).

Halogen Substitution Products of the β-Ketonic Esters

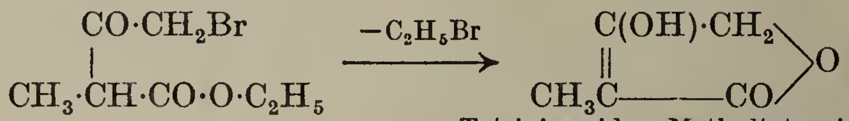
Chlorine alone or in the presence of sulphuryl chloride acting on acetoacetic ester replaces the hydrogen atoms both of the CH_2 and CH_3 groups by chlorine. The hydrogen of the CH_2 group is first substituted.

α-*Chloroacetoacetic ester.* $CH_3COCHClCO_2C_2H_5$, b.p. 109°/10 mm., possesses a penetrating odour. γ-*Chloroacetoacetic ester*, $ClCH_2COCH_2CO_2C_2H_5$, b.p. 105°/11 mm., is prepared by the oxidation of γ-chloro-β-hydroxybutyric ester with chromic acid; also synthetically, from chloroacetic ester and aluminium amalgam. *Copper salt*, m.p. 168° (decomp.) forms green crystals (C. 1904, I. 788: 1907, I. 944). α-*Bromoacetoacetic ester*, $CH_3CO\cdot CHBr\cdot CO_2C_2H_5$, b.p. 101–104°/12 mm., is obtained from acetoacetic ester and bromine in the cold (Ber. **36**, 1730). HBr converts it gradually into γ-*bromoacetoacetic ester*, $CH_2Br\cdot CO\cdot CH_2CO_2C_2H_5$, b.p. 125°/9 mm. (Ber. **29**, 1042). This substance is also formed from bromoacetic ester and magnesium (Ber. **41**, 954).

The constitution of these two bodies has been established by condensing them with thiourea to the corresponding thiazole derivatives.

αα-*Dichloroacetoacetic ester*, $CH_3COCCl_2CO_2C_2H_5$, b.p. 205°, is a pungent-smelling liquid. Heated with HCl it decomposes into α-dichloroacetone, $CH_3\text{-}COCHCl_2$, alcohol, and CO_2; with alkalis it yields acetic and dichloroacetic acids. αα-*Dibromoacetoacetic ester* is a liquid; it yields the *dioxime*, $CH_3C(NOH)\text{-}C(NOH)CO_2C_2H_5$, m.p. 142°. αγ-*Dibromoacetoacetic ester*, $CH_2Br\cdot CO\cdot CHBr\cdot CO_2C_2H_5$, m.p. 45–49°.

According to Demarçay (Ber. **13**, 1479, 1870) the γ-*bromo-mono-alkylaceto-acetic esters*, when heated alone or with water, split off ethyl bromide and yield peculiar acids; thus, bromomethyl acetoacetic ester gave tetrinic acid or methyltetronic acid, whilst bromoethyl acetoacetic ester yielded pentinic acid or ethyltetronic acid (*L. Wolff*, Ann. **291**, 226):

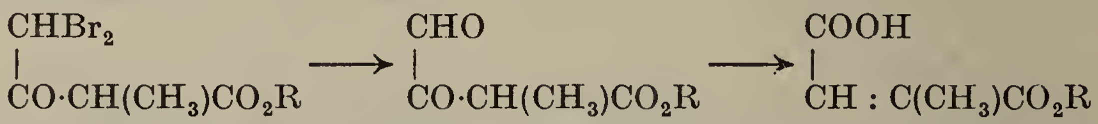


Tetrinic acid = Methyltetronic acid.

These acids will be discussed later as lactones of hydroxy-ketonic acids, together with the oxidation products of triacid alcohols.

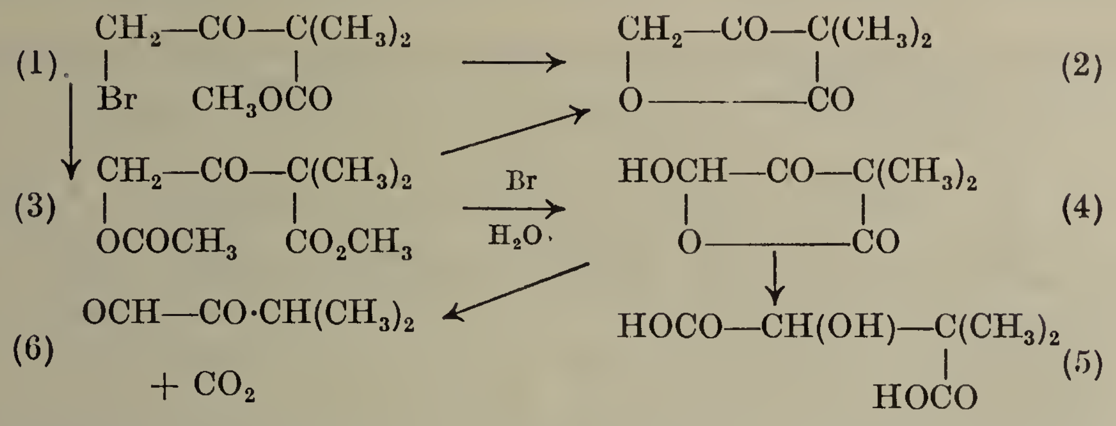
The γ-*dibromo-mono-alkyl acetoacetic esters*, treated with alcoholic potassium hydroxide, yield hydroxytetrinic acid, hydroxypentinic acid, etc. Gorbow (Ber. **21**, R. 180) found them to be homologues of fumaric acid. Hydroxytetrinic acid is mesaconic acid (*q.v.*); whilst hydroxypentinic acid is ethyl fumaric acid (*q.v.*), etc.

The formation of these olefine dicarboxylic acids from γγ-dibromo-mono-alkyl acetoacetic esters is easily explained on the assumption that the keto- or aldehyde acids are first formed, which are then converted into the unsaturated dicarboxylic acids:



$$\begin{array}{l} CHBr_2 \\ | \\ CO\cdot CH(CH_3)CO_2R \end{array} \longrightarrow \begin{array}{l} CHO \\ | \\ CO\cdot CH(CH_3)CO_2R \end{array} \longrightarrow \begin{array}{l} COOH \\ | \\ CH : C(CH_3)CO_2R \end{array}$$

The γ-*bromo-dialkyl acetoacetic esters*, however, behave differently, giving rise to lactones of γ-hydroxy-β-ketone carboxylic acids (Conrad and Gast). The bromine atom of the γ-bromo-dimethyl-acetoacetic ester (1, below), can be replaced by acetoxyl, producing the γ-acetoxy-dimethyl-acetoacetic ester (3), which gives up methyl acetate and changes into γ-hydroxy-dimethyl-acetoacetic acid lactone (2). Bromine, entering the molecule of the γ-acetoxy-dimethyl-acetoacetic ester, becomes attached to the γ-carbon atom, producing a compound which has not been isolated. The action of water on this is the immediate production of the lactone of γ-dihydroxy-dimethyl-acetoacetic acid (4). Its salts are those of an aldehyde-ketone-carboxylic acid, which is converted by alkalis into β-dimethyl malic acid (5); whilst on fusion a keto-aldehyde—*iso*butyryl-formaldehyde (p. 400)—is formed (6). The inter-relations of these compounds are shown as follows (Ber. **31**, 2726, 2954):

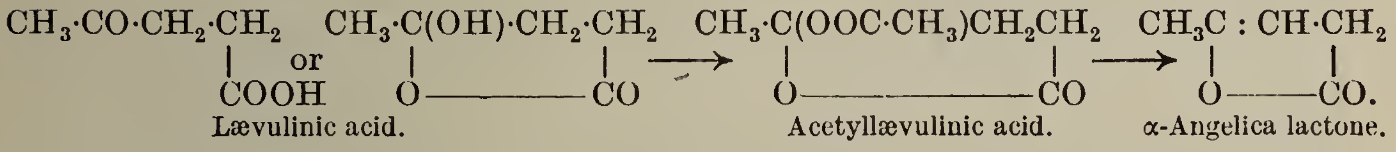


The action of ammonia on γ-bromo-dimethyl-acetoacetic ester to form the lactam of γ-amino-dimethyl-acetoacetic acid—dimethyl ketopyrrolidone—which is broken down by hydrochloric acid into amino-dimethyl-acetone (p. 397) (Ber. **32**, 1199).

γ-Trichloroacetoacetic ester, $CCl_3COCH_2CO_2C_2H_5$, b.p. 234°, is also prepared synthetically from chloral and diazoacetic ester (p. 459) (Ber. **40**, 3001).

III. γ-Ketonic Acids

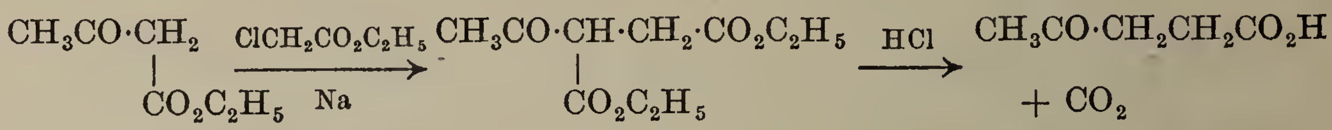
These acids are distinguished from the acids of the β-variety by the fact that when heated they do not yield CO_2, but split off water and pass into unsaturated γ-lactones. They form γ-hydroxy-acids on reduction, which readily pass into saturated γ-lactones. An interesting fact in this connection is that they yield remarkably well crystallized acetyl derivatives when treated with acetic anhydride. This reaction, as well as the production of unsaturated γ-lactones, on distillation suggests the possible formulation of the γ-ketonic acid as the tautomeric γ-hydroxylactones. Spectroscopic investigations have shown that free lævulinic acid possesses the open-chain keto-formula, while the acetyl derivative corresponds to the hydroxylactone structure (v. Auwers, Ber. **52**, 584):



Lævulinic acid, *β-acetopropionic acid, γ-ketovaleric acid,* [4-pentanone acid], $C_5H_8O_3 = CH_3·CO·CH_2·CH_2·CO_2H$, or $CH_3·\overbrace{C(OH)·CH_2·CH_2COO}$, m.p. 32·5°; b.p. 144°/12 mm., b.p. 239°/760 mm., with slight decomposition, is isomeric with methylacetoacetic acid, which may be designated α-acetopropionic acid.

(1) Lævulinic acid can be obtained from the hexoses (*q.v.*) on boiling them with dilute hydrochloric or sulphuric acid. It is more easily obtained from lævulose—hence the name—than from glucose. It is prepared by heating sucrose or starch with hydrochloric acid (Ber. **19**, 707, 2572: **20**, 1775: Ann. **227**, 99). Its constitution is evident from its direct and also indirect syntheses; (2) from the mono-ethyl ester of succinyl monochloride, $ClCO·CH_2·CH_2CO_2C_2H_5$, and zinc methyl (C. 1899, II. 418); and by boiling the reaction-product of chloroacetic ester and sodium acetoacetic ester—aceto-

succinic ester—with hydrochloric acid or barium hydroxide solution (*Conrad,* Ann. **188,** 223):



$$\underset{CO_2C_2H_5}{CH_3CO\cdot CH_2}\xrightarrow[Na]{ClCH_2CO_2C_2H_5}\underset{CO_2C_2H_5}{CH_3CO\cdot CH\cdot CH_2\cdot CO_2C_2H_5}\xrightarrow{HCl}CH_3CO\cdot CH_2CH_2CO_2H + CO_2$$

It is also obtained (3) by the action of concentrated H_2SO_4 on methyl glutolactonic acid, $CH_3\overline{C(CO_2H)CH_2CH_2COO}$; (4) by the oxidation of its corresponding γ-acetopropyl alcohol (p. 395), (5) by the oxidation of methylheptenone (p. 276), of linalool and geraniol, two bodies belonging to the group of olefine terpenes. (6) By hydrolysis of crotonaldehyde cyanohydrin with warm hydrochloric acid and the transformation of the propenyl glycollic acid thus formed (p. 452).

Lævulinic acid dissolves very readily in water, alcohol and ether, and undergoes the following changes: (1) By slow distillation under the ordinary pressure it breaks down into water and α- and β- angelic lactones (p. 453). (2) When heated to 150–200° with hydriodic acid and phosphorus, lævulinic acid is changed to *n*-valeric acid. (3) By the action of sodium amalgam sodium γ-hydroxyvalerate is produced, the acid from which changes into γ-valerolactone. (4) Dilute nitric acid converts lævulinic acid partly into acetic and malonic acid and partly into succinic acid and carbon dioxide. The action of sunlight on an aqueous solution of the acid is to produce a certain quantity of methyl alcohol, formic and propionic acids (Ber. **40,** 2417).

(5) Bromine converts the acid into substitution products (p. 479).

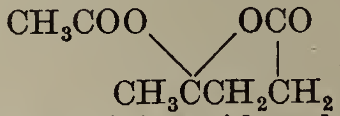
(6) Iodic acid changes it to bi-iodo-acetoacrylic acid.

(7) P_2S_3 converts it into thiotolen, $C_4H_3S\cdot CH_3$ (Vol. III). For the behaviour of lævulinic acid with hydroxylamine and phenylhydrazine consult the paragraph relating to the nitrogen derivatives of the γ-ketonic acids.

Nucleus-synthetic Reactions: (8) Hydrocyanic acid and lævulinic acid yield the nitrile of methyl glutolactonic acid: $CH_3\cdot\overline{C(CN)CH_2CH_2COO}$ (see above). (9) Benzaldehyde and lævulinic acid condense in acid solution to β-benzal lævulinic acid, and in alkaline solution to δ-benzal lævulinic acid (Ann. **258,** 129: Ber. **26,** 349). (10) Electrolysis of potassium lævulinate results in the production of $\alpha\delta$-diacetyl butane (p. 405) (Ber. **33,** 155).

Lævulinic Acid Derivatives.—The *calcium salt* $(C_5H_7O_3)_2Ca + 2H_2O$; *silver salt,* $C_5H_7O_3Ag$, is a characteristic, crystalline precipitate, dissolving in water with difficulty; *methyl ester,* $C_5H_7(CH_3)O_3$, b.p. 191°; *ethyl ester,* b.p. 200°: *phenylhydrazone,* m.p. 103°.

Acetyllævulinic acid, γ-acetoxyl-γ-valerolactone,



$$\begin{array}{l} CH_3COO\diagdown\ \diagup OCO \\ \qquad CH_3CCH_2CH_2 \end{array}$$

, m.p. 78°, is particularly noteworthy. It is formed from lævulinic acid and acetic anhydride; from silver lævulinate and acetyl chloride; from lævulinic chloride and silver acetate; as well as from α-angelic lactone and acetic acid. The last method of formation, as well as the formation of α- and β-angelic lactone by heating acetolævulinic acid are most easily understood upon the assumption that the constitution is really as indicated in the formula shown above. Spectroscopic data also support the acetoxylactone formula for the compound (Ann. **256**, 314 : Ber. **52**, 584).

Lævulinic chloride, γ-chlorovalerolactone, $CH_3CClCH_2CH_2COO$, b.p. 80°/15 mm., is produced by the addition of HCl to α-angelic lactone, and by the action of acetyl chloride on lævulinic acid (Ann. **256**, 334). *Lævulinamide, γ-aminovalerolactone*, $CH_3C(NH_2)CH_2CH_2COO$, m.p. 107°, has been obtained from lævulinic ester, and from α-angelic lactone and ammonia (Ann. **229**, 249).

Homologous lævulinic acids are obtained from the homologues of acetosuccinic ester (p. 622) :

β-Methyllævulinic acid, β-acetobutyric acid, $CH_3CO{\cdot}CH(CH_3)CH_2CO_2H$, m.p. − 12°, b.p. 242°, is prepared from α-methylacetosuccinic ester. It forms a difficultly soluble semicarbazone (C. 1900, II. 242), *α-methyllævulinic acid, β-acetyl*iso*butyric acid*, $CH_3CO{\cdot}CH_2CH(CH_3)CO_2H$, m.p. 248°. *Homolævulinic acid, δ-methyllævulinic acid*, $CH_3CH_2CO{\cdot}CH_2CH_2COOH$, m.p. 32°, is obtained from βγ-dibromocaproic acid (Ann. **268**, 69), together with one of the hydroxycaprolactones. *α-Ethyllævulinic acid*, $CH_3CO{\cdot}CH_2CH(C_2H_5)CO_2H$, m.p. 250–252°.

Mesitonic acid, αα-dimethyllævulinic acid, $CH_3CO{\cdot}CH_2C(CH_3)_2CO_2H$, m.p. 74°, b.p. 138°/15 mm., is obtained by the action of alcoholic potassium cyanide solution on mesityl oxide, $CH_3COCH : C(CH_3)_2$ (p. 273). The *nitrile*, $CH_3COCH_2(CH_3)_2CN$, is formed as an intermediate product, and can be formed from mesityl oxide hydrochloride by KCN. Mesityl oxide and hydrocyanic acid in excess produce the cyanohydrin of mesitonic nitrile, the dinitrile of the so-called mesitylic acid, which decomposes on being heated with hydrochloric acid into formic and mesitonic acids (C. 1904, II. 1108 : Ber. **37**, 4070 : Ann. **247**, 90). Mesitonic acid is converted into dimethylmalonic acid when oxidized with nitric acid.

ββ-Dimethyllævulinic acid, $CH_3COC(CH_3)_2{\cdot}CH_2CO_2H$, b.p. 151°/18 mm., results from α-*unsym.*-dimethylsuccinyl chloride and zinc methyl (C. 1899, II. 524).

δδ-Dimethyllævulinic acid, $(CH_3)_2CH{\cdot}CO{\cdot}CH_2CH_2CO_2H$, m.p. 40°, is prepared from the result of the double decomposition of γ-bromo-dimethyl-acetoacetic ester and sodium malonic ester, by heating it with dilute sulphuric acid (Ber. **30**, 864) ; by oxidation of dimethylacetonylacetone (p. 405) (Ber. **31**, 2311) ; from dibromo-*iso*heptoic acid and soda solution (Ann. **288**, 133) ; by oxidation of various terpene derivatives (Vol. II), such as thujone.

βδ-Dimethyllævulinic acid, $CH_3CH_2COCH(CH_3)CH_2COOH$, b.p. 154°, is produced from γ-ethylidene-β-methyl butyrolactone, a degradation product of dicrotonic acid (*q.v.*) ; also by the splitting-up of αα¹-dimethylacetonedicarboxylic-α-acetic ester (Ber. **33**, 3323).

Caproyl iso*butyric acid*, $C_5H_{11}COCH_2CH(CH_3)CO_2H$, m.p. 33°, b.p. 190°/33 mm. (C. 1905, II. 1782).

Halogen γ-Ketonic Acids.—*α-Bromolævulinic acid*, $CH_3COCH_2CHBrCO_2H$, m.p. 79°, is produced when HBr acts on β-acetoacrylic acid. Boiling water converts it into α-hydroxylævulinic acid (*q.v.*).

β-Bromolævulinic acid, $CH_3COCHBrCH_2CO_2H$, m.p. 59°, is produced in the bromination of lævulinic acid, as well as by the action of water on the addition product of bromine and α-angelic lactone. Warming with sodium hydroxide converts the β-bromolævulinic acid into α-hydroxylævulinic acid and β-acetoacrylic acid. Ammonia converts the β-bromolævulinic acid into tetramethyl pyrazine, whilst aniline produces 2,3-dimethylindole (Ber. **21**, 3360).

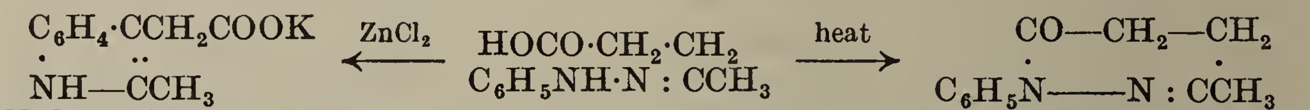
αβ-Dibromolævulinic acid, $CH_3COCHBrCHBrCO_2H$, m.p. 108°, is prepared from β-acetoacrylic acid and Br_2. *βδ-Dibromolævulinic acid*, $CH_2BrCOCHBrCH_2CO_2H$, m.p. 115°, is produced in the bromination of lævulinic acid. It yields diacetyl and glyoxylpropionic acid, $HOC{\cdot}CO{\cdot}CH_2CH_2CO_2H$, when it is boiled with water. Concentrated nitric acid converts it into dibromodinitromethane and monobromosuccinic acid, whilst with concentrated sulphuric acid it yields two isomeric dibromo*cyclo*pentenediones (Vol. II).

Nitrogen Derivatives of the γ-Ketonic Acids.

(1) *Lævulinamide*, $CH_3COCH_2CH_2CONH_2$ or $CH_3C(NH_2)CH_2CH_2COO$, m.p. **107°** (see above).

(2) *Action of hydrazine*, NH_2NH_2: *Lævulinic hydrazide*, $CH_3COCH_2CH_2\cdot CONHNH_2$, m.p. 82°. On the application of heat it passes into a lactazam (p. 461)—3-*methylpyridazinone*, $CH_3(C{=}N\cdot NH)CH_2CH_2CO$, m.p. 94° (Ber. **26**, 408; J. pr. Chem. [2] **50**, 522).

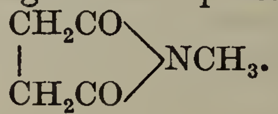
(3) *Action of phenylhydrazine*, $NH_2NHC_6H_5$: The first product is a hydrazone, which yields a lactazam when heated. *Lævulinic phenylhydrazone*, $CH_3C({=}NNHC_6H_5)CH_2CH_2CO_2H$, m.p. 108°. This passes into 3-*methylphenylpyridazolone*, m.p. 81° (Ann. **253**, 44). When fused with zinc chloride it becomes 2-methylindoleacetic acid,



Methylindoleacetic acid. Methylphenylpyridazolone.

Mesitonic acid phenylhydrazone, $CH_3C(:NNHC_6H_5)CH_2C(CH_3)_2CO_2H$, m.p. 121·5°, passes into *trimethyl-N-phenylpyridazolone*, $C_6H_5NN{:}C(CH_3)CH_2C(CH_3)_2CO$, m.p. 84° (Ann. **247**, 105).

(4) *Action of hydroxylamine*: *Lævulinic oxime*, $CH_3C(NOH)CH_2CH_2CO_2H$, m.p. 95° (Ber. **25**, 1930), undergoes rearrangement in presence of concentrated sulphuric acid into succinyl methylimide,



$$\begin{matrix}CH_2CO\\ |\\ CH_2CO\end{matrix}\!\!>\!NCH_3.$$

IV. δ-Ketonic Acids, etc.

Such acids have been prepared from acetylglutaric acids (*q.v.*) by the elimination of CO_2. On reduction they yield δ-lactones (p. 428).

γ-Acetobutyric acid, $CH_3CO\cdot CH_2CH_2CH_2CO_2H$, m.p. 13°, b.p. 275°, is formed by the oxidation of δ-acetobutyl alcohol (p. 395); and from dihydroresorcinol by barium hydroxide solution. Sodium ethoxide changes it back into dihydroresorcinol.

γ-Ethyl-γ-acetobutyric acid, $CH_3CO\cdot CH(C_2H_5)CH_2CH_2CO_2H$, b.p. 173°/10 mm., b.p. 280°. *γγ-Dimethyl-γ-acetobutyric acid*, $CH_3\cdot COC(CH_3)_2CH_2CH_2COOH$, m.p. 48°, is obtained from αα-dimethylglutaric ethyl ester acid chloride and zinc methyl (C. 1899, II. 524); also from *iso*lauronolic acid and β-campholenic acid by oxidation (C. 1897, I. 26). *γ-Butyrobutyric acid*, $CH_3CH_2CH_2CO\cdot CH_2CH_2\cdot CH_2CO_2H$, m.p. 34°, from coniine (Vol. III) and H_2O_2.

Certain higher ketonic acids have been prepared by the oxidation of hydroaromatic compounds of the terpene group, and are important in determining the constitution of the latter. Other ketonic acids result from the hydration of acetylene carboxylic acids by means of concentrated sulphuric acid. A case in point is ketostearic acid, from stearolic acid (p. 352), which is produced on treating oleic and elaidic di-bromides with alcoholic potassium hydroxide. See oleic acid (p. 348) for the value of these ketonic acids in determining the constitution of the olefine and acetylene carbonic acids, which are closely related to them.

*β-iso*Propyl-δ-acetyl valeric acid, $CH_3CO\cdot CH_2\cdot CH_2CH(C_3H_7)CH_2CO_2H$, m.p. 40°, b.p. 192°/20 mm., is prepared from tetrahydrocarvone (Vol. II). *β-Methyl-δ-*iso*butyrylvaleric acid*, $CH_3CH(CH_3)CO\cdot CH_2CH_2CH(CH_3)CH_2CO_2H$, b.p. 186°/20 mm., is prepared from menthone (Vol. II). *Undecanonic acid*, $CH_3CO\cdot[CH_2]_8CO_2H$ (?), m.p. 49°, is formed from undecolic acid (p. 352).

θ-Ketostearic acid, $CH_3[CH_2]_8CO[CH_2]_7CO_2H$, m.p. 83°, is obtained from chloroketostearic acid (Ber. **29**, 806), and is a transposition product of ricinoleic acid (p. 354).

ι-Ketostearic acid, $CH_3[CH_2]_7CO[CH_2]_8CO_2H$, m.p. 76°, is obtained from stearolic acid (p. 352) by the action of concentrated sulphuric acid; also by heating the salt of dihydroxystearic acid, produced by the oxidation of this acid by $KMnO_4$ (J. pr. Chem. [2] **71**, 422). Consult oleic acid (p. 348) for the decomposition of its oxime.

B. UNSATURATED KETONIC ACIDS

(i) Ketencarboxylic Acids

Ethylketencarboxylic Acid. The *ethyl ester*, $C_2H_5(C_2H_5{\cdot}CO_2)C:CO$, b.p. 48°/15 mm., is a colourless liquid, obtained from ethylbromomalonic chlorides and zinc and distillation of its polymer, diethyl*cyclo*butanedionedicarboxylic ester under 15 mm. pressure (Ber. **42**, 4908).

Ketenacetalcarboxylic ester (*diethoxyacrylic ester*), $C_2H_5CO_2{\cdot}CH:C(OEt)_2$, b.p. 128°/12 mm., is a highly refractive liquid, obtained from cyanoacetic ester by way of the imidoether and orthoether by distillation under 12 mm. (Reitter and Weindel, Ber. **40**, 3360). *α-Chloro-β-diethoxyacrylic ester*, $C_2H_5CO_2{\cdot}CCl:C(OEt)_2$, b.p. 157–159°/50 mm., is obtained from trichloroacrylic ester and sodium ethoxide (Ann. **297**, 319).

(ii) Olefineketonecarboxylic Acids

β-Ketonic Acids.—*Ethylideneacetoacetic ester*, $CH_3{\cdot}CO{\cdot}C(:CHCH_3)COOH$, b.p. 211°, results from the action of hydrochloric acid, ammonia, diethylamine or piperidine on aldehyde and acetoacetic ester (Ann. **218**, 172 : Ber. **29**, 172 : **31**, 735). Magnesium methyl iodide converts it into a salt of *iso*propylacetoacetic ester (C. 1902, I. 1197).

iso*Propylideneacetoacetic ester*, $CH_3CO{\cdot}C(:CMe_2)COOH$, b.p. 215°, is prepared from acetone and acetoacetic ester by the action of HCl and then of quinoline (Ber. **30**, 481).

iso*Heptenoylacetic acid*, $(CH_3)_2C:CCH_2CH_2COCH_2CO_2H$, is prepared from *iso*hexenylpropiolic acid (method of formation 5, p. 469); *ethyl ester*, b.p. 127–130°/14 mm. (C. 1903, I. 1019).

γ-Ketonic Acids : *β-Acetoacrylic acid*, $CH_3CO{\cdot}CH:CHCO_2H$, m.p. 125°, is derived together with β-hydroxylævulinic acid from β-bromolævulinic acid, and also from chloralacetone upon digestion with a soda solution. It combines with bromine and with hydrobromic acid, forming αβ-dibromolævulinic acid and α-bromolævulinic acid (Ann. **264**, 234). For constitution of β-acetoacrylic acid, see Ber. **35**, 1157.

β-Trichloroacetoacrylic acid, trichlorophenomalic acid, $CCl_3CO{\cdot}CH:CHCO_2H$, or $CCl_3{\cdot}\overline{C(OH)CH:CHCOO}$, m.p. 131°, is obtained from benzene by the action of potassium chlorate and sulphuric acid (Ann. **223**, 170 : **239**, 176). It breaks up into chloroform and maleic acid when boiled with barium hydroxide. It yields *acetyltrichlorophenomalic acid*, $CCl_3\overline{C(OCOCH_3)CH:CH{\cdot}COO}$, m.p. 86° (Ann. **254**, 152), when treated with acetic anhydride. *Perchloroacetylacrylic acid*, $CCl_3COCCl:CCl{\cdot}CO_2H$, m.p. 83–84° (Ber. **26**, 511), and other chlorinated acetyl acrylic and acetyl methyl acrylic acids (Ber. **26**, 1670), are formed from the decomposition of benzene derivatives which have previously been chlorinated.

αβ-Dibromo-β-acetylacrylic acid, $CH_3CO{\cdot}CBr:CBrCOOH$, or $CH_3{\cdot}\overline{C(OH)CBr:CBrCOO}$, m.p. 78°, results upon treating α-tribromothiotolen with nitric acid. Its remarkably low conductivity points to a lactone formula (Ber. **24**, 77 : **26**, R. 16).

δ-Ketonic Acids.—Chlorinated δ-ketonic acids have been obtained from the ketochlorides of resorcinol and orcinol, *e.g.* trichloroacetyltrichlorocrotonic acid, $CCl_3CO{\cdot}CCl:CHCCl_2CO_2H$ (Ber. **26**, 317, 504, 1666).

CARBONIC ACID AND ITS DERIVATIVES

The salts and esters of carbonic acid are derived from an acid of the formula $CO(OH)_2$, which, although it may be regarded as hydroxyformic acid, differs sufficiently from the other hydroxy acids to merit separate treatment. It behaves as a weak dibasic acid. The free acid, like most compounds containing two —OH groups attached to the same carbon atom, is unstable, and breaks down on liberation into the anhydride, carbon dioxide, CO_2, and water. Derivatives of orthocarbonic acid, $C(OH)_4$, are known, but the free acid, like metacarbonic acid (ordinary carbonic acid), breaks down immediately on liberation into $CO_2 + 2H_2O$.

In the system on which this book is arranged, all compounds derived from methane by the replacement of all four hydrogen atoms by monovalent residues can be regarded as derivatives of orthocarbonic acid, and such compounds as chloropicrin, CCl_3NO_2, tetranitromethane, $C(NO_2)_4$, will be treated as such. The tetraamino derivative $C(NH_2)_4$ does not exist, but in reactions where it is expected, ammonia is liberated and guanidine, $(NH_2)_2C : NH$, is formed.

Carbon dioxide, CO_2, is the final combustion product of carbon. Under favourable conditions the carbon of every organic substance will be converted into it. In the quantitative analysis of carbon derivatives carbon is determined in the form of CO_2 (p. 2).

Liquid carbon dioxide is a good solvent for many organic substances, especially those that are more volatile, a behaviour which resembles the organic solvents (C. 1906, I. 1239).

Several of the methods for the formation of carbon dioxide, which are especially important in organic chemistry, may be mentioned here. Carbon dioxide is developed from fermentable sugars in the alcoholic fermentation process (p. 140). It is readily formed by the oxidation of formic acid (p. 280), into which it can be converted by reduction (Ber. 28, R. 458); and can be withdrawn from the carboxylic acids containing the carboxyl group, $-C\leqslant^{OH}_{O}$, when hydrogen will enter where the carboxyl group was first attached. Those polycarboxylic acids, containing two carboxyl groups in union with each other, or two and more carboxyls linked to the same carbon atom, readily part with carbon dioxide on the application of heat. In the latter case carboxylic acids result, in which each carboxyl surviving is attached to a separate carbon atom, *e.g.*:

Malonic acid, $HO_2C{\cdot}CH_2{\cdot}CO_2H \longrightarrow CO_2 + CH_3{\cdot}CO_2H$.

The β-ketonic acids behave similarly (p. 466), losing CO_2 and yielding ketones:

Acetoacetic acid, $CH_3COCH_2{\cdot}CO_2H \longrightarrow CO_2$ and $CH_3CO{\cdot}CH_3$.

Monocarboxylic acids or their alkali salts can be deprived of CO_2 upon heating them with NaOH, when it is withdrawn as Na_2CO_3 (p. 96):

$$CH_3CO_2Na + NaOH = Na_2CO_3 + CH_4.$$

The electric current, acting on concentrated solutions of the alkali salts of carboxylic acids, splits off carbon dioxide (p. 94), *e.g.*:

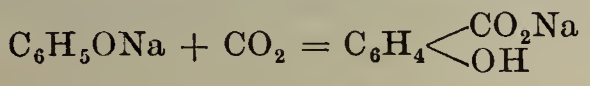
$$2CH_3CO_2K \longrightarrow \overbrace{CH_3CH_3 + 2CO_2}^{+} \text{ and } 2K.$$

The calcium salts of many carboxylic acids are decomposed by heat with the production of calcium carbonate and ketones (p. 256), *e.g.*:

$$(CH_3CO_2)_2Ca \longrightarrow CaCO_3 + CH_3COCH_3.$$

These and similar reactions, in which CO_2 readily separates from organic compounds, are of the first importance in the production of the different classes of compounds. In contrast to the splitting-off of CO_2 in certain reactions we have its absorption by certain organic metallic derivatives: nucleus-syntheses, in which carboxylic acids are produced:

$$CH_3MgI + CO_2 = CH_3CO_2MgI; \quad CH_3C\vdots CNa + CO_2 = CH_3C\vdots CCO_2Na;$$



$$C_6H_5ONa + CO_2 = C_6H_4{<}\genfrac{}{}{0pt}{}{CO_2Na}{OH}$$ (*cf. Salicylic Acid*, Vol. II).

Esters of Metacarbonic Acid, or ordinary Carbonic Acid

The **primary esters** of carbonic acid are not stable in a free condition. They are prepared from the alcohols and carbon dioxide at low temperatures (Ber. **31**, 3001).

Dumas and Peligot obtained the barium salt of methyl carbonic acid on conducting carbon dioxide into a methyl alcohol solution of anhydrous barium hydroxide (Ann. **35**, 283).

Magnesium methoxide combines with CO_2 to form magnesium methyl carbonate (Ber. **30**, 1836).

The potassium salt of ethyl carbonic acid, $C_2H_5O{\cdot}CO{\cdot}OK$, separates in pearly scales on adding CO_2 to the alcoholic solution of potassium alcoholate. Water decomposes it into potassium carbonate and alcohol.

The **neutral esters** are formed (1) when the alkyl iodides act on silver carbonate:

$$Ag_2CO_3 + 2C_2H_5I = (C_2H_5)_2CO_3 + 2AgI;$$

also (2) by treating esters of chloroformic acid with alcohols, whereby *mixed esters* may also be obtained:

$$CH_3OCOCl + HOC_2H_5 = \underset{\text{Methyl ethyl carbonate.}}{CH_3O{\cdot}CO{\cdot}OC_2H_5} + HCl.$$

On application of heat, the higher alcohols are able to expel the lower alcohols from the mixed esters:

$$\underset{\text{Methyl ethyl ester.}}{C_2H_5OCOOCH_3} + C_2H_5{\cdot}OH = \underset{\text{Diethyl ester.}}{C_2H_5OCOOC_2H_5} + CH_3OH.$$

Hence, to obtain the mixed ester, the reaction must occur at a lower temperature.

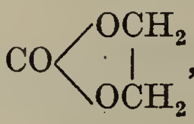
As regards the nature of the product, it is immaterial as to what order is pursued in introducing the alkyl groups, *i.e.* whether proceeding from chloroformic ester, we let ethyl alcohol act on it, or reverse the case, letting methyl alcohol act on ethyl chloroformic ester ; the same methyl ethyl carbonate results in each case (Ber. **13**, 2417).

The neutral carbonic esters are ethereal-smelling liquids, dissolving readily in water. Excepting the dimethyl and the methyl ethyl ester, all are lighter than water. With ammonia they first yield carbamic esters and then urea. When they are heated with phosphorus pentachloride, an alkyl group is eliminated, and in the case of the mixed esters this is always the lower one, whilst the chloroformic esters constitute the product :

$$C_2H_5OCOOCH_3 + PCl_5 = C_2H_5OCOCl = POCl_3 + CH_3Cl.$$

Carbonic esters are converted to carboxylic esters by alkyl and aryl-magnesium halides (Ber. **38**, 561).

Methyl carbonate, $CO(OCH_3)_2$, b.p. 91°, is produced from chloroformic ester by heating it with lead oxide ; *methyl ethyl ester*, $CH_3OCOOC_2H_5$, b.p. 109° ; *diethyl ester*, $CO(OC_2H_5)_2$, b.p. 126°, is obtained from ethyl oxalate, on warming with sodium or sodium ethoxide (with evolution of CO) ; *methyl propyl ester*, b.p. 131°.

Glycol carbonate, ethylenecarbonate,  $CO\left\langle\begin{matrix}OCH_2\\ |\\ OCH_2\end{matrix}\right.$, m.p. 39°, b.p. 236°, is obtained from glycol and $COCl_2$.

Derivatives of Orthocarbonic Acid (p. 482)

Orthocarbonic esters or *tetrabasic carbonic esters* (*Bassett*, Ann. **132**, 54), are produced when sodium alcoholates act on chloropicrin :

$$CCl_3(NO_2) + 4C_2H_5ONa = C(OC_2H_5)_4 + 3NaCl + NaNO_2.$$

Ethyl orthocarbonate, $C(OC_2H_5)_4$, b.p. 158°, is a liquid with an ethereal odour. When heated with ammonia it yields guanidine (p. 512) and alcohol. Alkyl and aryl magnesium halides convert it to ortho-carboxylic esters, $RC(OC_2H_5)_3$ (p. 330) (Ber. **38**, 563).

The *propyl ester*, $C(OC_3H_7)_4$, b.p. 224° ; iso*butyl ester*, b.p. 245° ; *methyl ester*, m.p. — 5·5°, b.p. 114°, is obtained from chloropicrin and sodium methoxide (Ber. **60**, 1841).

The tetrahalogen substitution products of methane can be regarded as the halides corresponding with orthocarbonic acid. They bear the same relation to the orthocarbonic esters that chloroform, bromoform and iodoform sustain to the orthoformic esters. Indeed, tetrachloro- and tetrabromomethane and sodium alcoholate do yield orthocarbonic esters, though with poor yield (Ber. **38**, 563 : C. 1906, I. 1691). The formation of orthocarbonic esters from trichloromethyl sulphochloride (p. 490) by means of $NaOC_2H_5$, see C. 1908, I. 1041.

Tetrahalogen Substitution Products of Methane

Tetrafluoromethane, *carbon tetrafluoride*, CF_4, is a colourless gas, condensable by pressure. This body belongs to that small class of carbon derivatives which can be directly prepared from the elements. Finely divided carbon, *e.g.* lamp black, combines directly with fluorine, with production of light and heat.

Tetrachloromethane, *carbon tetrachloride*, CCl_4, b.p. 76°, $D_0 = 1{\cdot}631$, is formed (1) by the action of chlorine on chloroform in sunlight, or upon the addition of iodine, and (2) by action of Cl on CS_2 at 20–40°, C_2Cl_4 and C_2Cl_6 being formed at the same time (Ber. **27**, 3160) ; (3) upon heating CS_2 with S_2Cl_2 in the presence of small quantities of iron: $CS_2 + 2S_2Cl_2 = CCl_4 + 6S$ (D.R.P. 72999). Preparation of the pure substance, see C. 1899, II. 1098.

It is a pleasant-smelling liquid solidifying to a crystalline mass at − 30°. It is an excellent solvent for many substances, and is made upon a technical scale. When heated with alcoholic KOH, it decomposes according to the following equation:

$$CCl_4 + 6KOH = K_2CO_3 + 3H_2O + 4KCl.$$

When the vapours are conducted through a red-hot tube, decomposition occurs, and C_2Cl_4 and C_2Cl_6 are produced. This is an interesting reaction because, as we have learned under acetic acid (p. 301), it plays a part in the first synthesis of this long-known acid. C_2Cl_6 is produced from CCl_4 by means of aluminium amalgam (p. 122). When carbon tetrachloride is digested with phenols and sodium hydroxide, phenolcarboxylic acids are produced (Vol. II).

Tetrabromomethane, CBr_4, m.p. 92·5°, b.p. 189°, obtained by the action of bromine iodide on bromoform or CS_2, or of bromine and alkali on acetone and other compounds (C. 1906, I. 1691), crystallizes in shining plates.

Tetraiodomethane, CI_4, $D_{20} = 4{\cdot}32$, is formed when CCl_4 is heated with aluminium iodide. It crystallizes from ether in dark-red, regular octahedra. On exposure to air it decomposes into CO_2 and I, a change which is accelerated by heat.

Nitro-derivatives of Orthocarbonic Acid

Nitrochloroform, *chloropicrin*, $C(NO_2)Cl_3$, b.p. 112°, $D_0 = 1{\cdot}692$, is frequently produced in the action of nitric acid on chlorinated carbon compounds such as chloral, and also when chlorine or bleaching powder acts on nitro-derivatives, picric acid and nitromethane; also from mercury fulminate (p. 294) and chlorine.

In the preparation of chloropicrin, 10 parts of bleaching powder are mixed to a thick paste with water. To this is added 1 part of picric acid or 2 : 4 : 6-trinitrophenol, $C_6H_2(OH)(NO_2)_3$.

Chloropicrin is a colourless liquid, possessing a very penetrating odour that attacks the eyes powerfully. It explodes when heated rapidly. When treated with acetic acid and iron filings it is converted into methylamine:

$$CCl_3(NO_2) + 6H_2 = CH_3{\cdot}NH_2 + 3HCl + 2H_2O.$$

Alkali sulphites change it to formyl trisulphonic acid, ammonia to guanidine, and sodium ethoxide to orthocarbonic ester.

Bromopicrin, $CBr_3(NO_2)$, m.p. 10°, can be distilled under greatly reduced pressure without decomposition, and is formed, like the preceding chloro-compound, by heating picric acid with calcium hypobromite (calcium hydroxide and bromine), or by heating nitromethane with bromine (p. 181). It is obtained in good yield by the action of bromine on aqueous picric acid in presence of sodium carbonate in sunlight. By the action of 50 per cent. potassium hydroxide it yields the yellow, explosive dipotassium derivative of *s*-tetranitroethane (J.C.S. **123**, 543). It closely resembles chloropicrin.

Bromonitroform, *tetranitromethane* and the salts of the nitroforms, which belong here, have already been described among the nitroparaffins (p. 186).

Chlorides of Carbonic Acid

As a dibasic acid, carbonic acid theoretically forms two acid chlorides. Of these, the monochloride, Cl·COOH, does not exist in the free condition, although derivatives such as esters are known. The dichloride, Cl·CO·Cl (phosgene), is capable of separate existence.

(1) Chlorocarbonic Esters (*Chloroformic Esters*).—The primary chloride of carbonic acid, chlorocarbonic acid, is not known, because it loses HCl too easily. Its esters are, however, known, and are produced when alcohols act on phosgene or carbon oxychloride, the secondary chloride of carbonic acid (Dumas, 1833). They are often called chloroformic esters, because they can be regarded as esters of the chlorine substitution products of formic acid:

$$COCl_2 + C_2H_5OH = ClCOOC_2H_5 + HCl.$$

They are most readily prepared by introducing the alcohol into liquid and strongly cooled phosgene (Ber. **18**, 1177). They are volatile, disagreeable-smelling liquids, decomposable by water, and when heated with anhydrous alcohols they yield the neutral carbonic esters; with ammonia they yield urethanes (p. 491); with hydrazine, hydrazicarbonic esters (p. 503); with ammonium azide, azidoformic esters (p. 503). They contain the group COCl, just as in acetyl chloride; hence they behave like fatty-acid chlorides.

The *methyl ester*, $Cl{\cdot}CO_2CH_3$, b.p. 71·4°; *ethyl ester*, b.p. 93°, $D_{15} = 1{\cdot}14$; *propyl ester*, b.p. 115°; iso*butyl ester*, b.p. 128·8°; iso*amyl ester*, b.p. 154° (Ber. **13**, 2417: **25**, 1449); *allyl ester*, b.p. 180° (Ann. **302**, 262).

Perchlorocarbonic ethyl ester, $Cl{\cdot}COOC_2Cl_5$, m.p. 26°, b.p. 83°/10 mm., b.p. 209°/760 mm., D = 1·737, is isomeric with perchloroacetic methyl ester (p. 335: Ann. **273**, 56).

Chlorocarbonate of glycollic ester, $Cl{\cdot}CO{\cdot}OCH_2CO_2C_2H_5$, b.p. 182°. *Chlorocarbonate of lactic ester*, $CH_3CH(OCOCl){\cdot}CO_2C_2H_5$, b.p. 91°/19 mm. (Ann. **302**, 262).

(2) **Carbonyl chloride**, *phosgene, carbon oxychloride*, $COCl_2$, b.p. 8°, was first obtained by Davy, in 1812, by the direct union of CO with Cl_2 in sunlight; hence the name phosgene, from φῶς, light, and γεννάω, to produce. It is also formed by conducting CO into boiling $SbCl_5$, and by oxidizing chloroform by air in the sunlight or with chromic acid:

$$2CHCl_3 + CrO_3 + 2O = 2COCl_2 + H_2O + CrO_2Cl_2.$$

Phosgene is most conveniently prepared from carbon tetrachloride (100 c.c.), and 80% "Oleum" (120 c.c.), a sulphuric acid containing SO_3 (Ber. **26**, 1990), when the SO_3 is converted into pyrosulphuryl chloride, $S_2O_5Cl_2$.

Technically it is made by conducting CO and Cl_2 over pulverized and cooled bone charcoal (*Paternò*).

Carbonyl chloride is a colourless gas, which on cooling is condensed to a liquid.

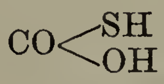
Reactions.—(1) Water slowly breaks it up into CO_2 and 2HCl. (2) Alcohols convert it into chlorocarbonic and carbonic esters. (3) With ammonium chloride it forms urea chloride. (4) Urea is produced when ammonia acts on it. Phosgene is employed in numerous nucleus-synthetic reactions, *e.g.* it is used technically for the preparation of di- and tri-phenylmethane dye-stuffs (see Tetramethyldiaminobenzophenone, Vol. II).

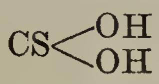
Carbonyl bromide, $COBr_2$, b.p. 64–65°, $D_{15} = 2{\cdot}45$, is prepared from carbon tetrabromide and concentrated sulphuric acid, at 150–160°. It is a colourless liquid which fumes in the air (Ann. **345**, 334).

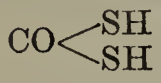
Carbonyl fluoride, COF_2, has not been obtained pure (J. pr. Chem. [2] **101**, 79).

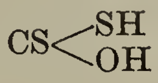
Sulphur Derivatives of Ordinary Carbonic Acid

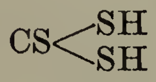
By supposing the oxygen in the formula $CO(OH)_2$ to be replaced by sulphur, there result:

1.  $CO\!<\!\begin{matrix}SH\\OH\end{matrix}$ Thiocarbonic acid. Carbonthiolic acid.

2.  $CS\!<\!\begin{matrix}OH\\OH\end{matrix}$ Sulphocarbonic acid. Carbonthionic acid.

3.  $CO\!<\!\begin{matrix}SH\\SH\end{matrix}$ Dithiocarbonic acid. Carbondithiolic acid.

4.  $CS\!<\!\begin{matrix}SH\\OH\end{matrix}$ Sulphothiocarbonic acid. Carbondithioic acid.

5.  $CS\!<\!\begin{matrix}SH\\SH\end{matrix}$ Trithicarbonic acid.

The doubly-linked *S* is indicated in the name by sulph or thion, whilst it is termed thio or thiol when singly linked.

The free acids are not known, or are very unstable, but numerous derivatives, such as salts, esters and amides, are known. Carbon oxysulphide, COS, is the anhydride or sulphanhydride corresponding with thiocarbonic acid, sulphocarbonic acid and dithiocarbonic acid.

Carbon disulphide, CS_2, sustains the same relation to sulphothiocarbonic acid and trithiocarbonic acid that carbon dioxide does to ordinary carbonic acid, while phosgene corresponds with thiophosgene, $CSCl_2$.

Carbon oxysulphide, COS (1867 *C. v. Than,* Ann. Spl. **5**, 245), occurs in some mineral springs as, for example, in the sulphur waters of Harkány and Parád in Hungary, and is formed (1) by conducting sulphur vapour and carbon monoxide through red-hot tubes; (2) on heating CS_2 with SO_3; (3) by the action of $COCl_2$ on CdS at 260–280° (Ber. **24**, 2971); (4) by the action of fatty acids (p. 322); or (5) sulphuric acid, diluted with an equal volume of water on potassium thiocyanate, $HSNC + H_2O = COS + NH_3$ (Ber. **20**, 550).

In order to obtain it pure (Ber. **36**, 1008) the gas may be conducted into an alcoholic potassium hydroxide solution, and (6) the separated potassium ethyl thiocarbonate, C_2H_5OCOSK, decomposed with dilute hydrochloric acid.

Carbon oxysulphide is a colourless gas, with a faint and peculiar odour. It inflames readily, and forms an explosive mixture with air. It is soluble in an equal volume of water, and in 6 volumes of toluene at 14°. It is decomposed by the alkalis according to the following equation:

$$COS + 4KOH = K_2CO_3 + K_2S + 2H_2O.$$

When heated to high temperatures it decomposes according to the equations (Ber. **52**, 681):

$$\text{(i) } 2COS \longrightarrow 2CO + S_2; \quad \text{(ii) } 2COS \longrightarrow CO_2 + CS_2.$$

Carbon disulphide, CS_2, b.p. 47°, D_0 1·297, was first obtained in 1796 by *Lampadius,* when he distilled pyrites with carbon. It is prepared by conducting sulphur vapour over ignited charcoal, and is one of the few carbon compounds which can be prepared by the direct union of carbon with other elements. It is a colourless liquid with strong refractive power. It is obtained pure by distilling the commercial product over mercury or mercuric chloride; its odour is then very faint. It is almost insoluble in water, but mixes with alcohol and ether. It serves as an excellent solvent for iodine, sulphur, phosphorus, fatty oils and resins, and is used in the vulcanization of rubber. In the cold it combines with water, yielding the *hydrate* $2CS_2 + H_2O$, which decomposes again at − 3°.

Small quantities of carbon disulphide are detected by conversion into potassium xanthate, by means of alcoholic potassium hydroxide, from which the copper salt is obtained. The production of the bright-red compound of CS_2 with triethylphosphine (p. 207, and Ber. **13,** 1732) is a more delicate test. Comp. also the mustard-oil reaction, p. 526.

H_2S and CS_2 conducted over heated copper yield methane (p. 92). Carbon disulphide is fairly stable towards dry halogens, so that it is frequently used as a solvent in adding halogens to unsaturated carbon compounds.

However, moist chlorine gas converts CS_2 into thiocarbonyl chloride, $CSCl_2$, and in the presence of iodine into CCl_3SCl, perchloromethyl mercaptan and S_2Cl_2; finally into CCl_4 (p. 484). Alcoholates change it into xanthates.

Thiocarbonic Acids.—The salts and esters of all these acids, which when free are exceedingly unstable, may be produced (1) by the union of the anhydrides, CO_2, COS, CS_2, with (*a*) the sulphides of the alkali and alkali earth metals, (*b*) the mercaptides of the alkali metals, (*c*) and of the last two with alcoholates; (2) by the transposition of the salts thus obtained with alkyl halides and alkylene dihalides; (3) by the action of alcohols and alcoholates, mercaptans and alkali mercaptides on $COCl_2$, $Cl{\cdot}CO_2C_2H_5$ (p. 485), $CSCl_2$ and $Cl{\cdot}CS_2C_2H_5$ (p. 490).

Monothiocarbonic Acids.

1. **Ethyl thiocarbonic acid, ethyl carbon-monothiolic acid,** $HS{\cdot}CO{\cdot}OC_2H_5$. The *potassium salt* (*Bender's salt*), $KS{\cdot}COOC_2H_5$, is obtained (1) from ethyl xanthic esters and alcoholic potassium hydroxide (p. 489), and (2) from carbon oxysulphide and alcoholic potassium hydroxide (J. pr. Chem. [2] **73,** 242). It forms prisms, easily soluble in water and alcohol, and produces a white precipitate with copper sulphate. With ethyl iodide its salt forms S-*ethyl thiocarbonate*, $C_2H_5S{\cdot}COOC_2H_5$, b.p. 156°, which can also be prepared from chlorocarbonic ester, $ClCOOC_2H_5$, and sodium or zinc mercaptide. Alkalis decompose it into carbonate, alcohol and mercaptan (Ber. **19,** 1227). *Thiodicarbonic ester*, $S(COOC_2H_5)_2$, b.p. 118°/22 mm., is produced from chlorocarbonic ester and Na_2S (J. pr. Chem. [2] **71,** 278).

2. **Sulphocarbonic acid,** *carbonthionic acid,* HOCSOH. Its *ethyl ester,* $CS(O{\cdot}C_2H_5)_2$, b.p. 161°, is produced by the action of sodium alcoholate on thiocarbonyl chloride, $CSCl_2$, and in the distillation of $S_2(CSOC_2H_5)$. It is an ethereal-smelling liquid. With alcoholic ammonia the ester decomposes into alcohol and ammonium thiocyanate, $CN{\cdot}S{\cdot}NH_4$.

Dithiocarbonic Acids.

3. **Dithiocarbonic acid,** *carbon-dithiolic acid,* $CO(SH)_2$. The free acid is not known.

The *methyl ester*, $CO(S{\cdot}CH_3)_2$, b.p. 169°, and *ethyl ester*, $CO(S{\cdot}C_2H_5)_2$, b.p. 196°, result (1) when $COCl_2$ acts on the mercaptides:

$$COCl_2 + 2C_2H_5{\cdot}SK = CO(S{\cdot}C_2H_5)_2 + 2KCl;$$

and (2) when thiocyanic esters (p. 525) are heated with concentrated sulphuric acid:

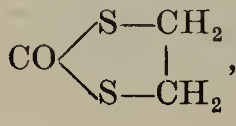
$$2CN{\cdot}S{\cdot}CH_3 + 3H_2O = CO(S{\cdot}CH_3)_2 + CO_2 + 2NH_2.$$

(3) from imido-dithio-carbonic ester (p. 506) and dilute hydrochloric acid (C. 1905, I. 447):

$$RN : C(SCH_3)_2 + H_2O = OC(SCH_3)_2 + RNH_2.$$

They are liquids with an odour of garlic. Alcoholic ammonia decomposes them into urea and mercaptans:

$$CO(S{\cdot}C_2H_5)_2 + 2NH_3 = CO(NH_2)_2 + 2C_2H_5{\cdot}SH.$$

Dithiocarbonic ethylene ester, , m.p. 310°, is produced from trithiocarbonic ethylene ester.

4. **Sulphothiocarbonic acid,** *carbondithioic acid,* $HO{\cdot}CS{\cdot}SH$, does not exist free. The xanthates or xanthogenates, $R{\cdot}O{\cdot}C{\cdot}SSM$, discovered by Zeise in 1824, are derived from it.

The *xanthogenates* are produced by the interaction of CS_2 and alkali hydroxides in alcoholic solution—*e.g.* potassium xanthate, consisting of yellow, silky needles, which crystallize :

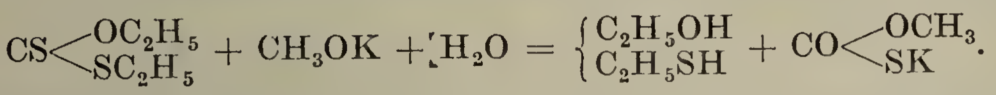
$$CS_2 + KOH + C_2H_5{\cdot}OH = \underset{\text{Potassium ethyl xanthate.}}{C_2H_5OCSSK} + H_2O.$$

Cupric salts precipitate *yellow cuprous* salts from solutions of the alkali xanthates together with disulphides $S_2(CSOR)_2$ (*cf.* Ber. **38,** 2184 : C. 1908, I. 1092). The acid owes its name, ξανθός, yellow, to this characteristic.

By the action of alkyl iodides on the salts the esters are formed. The latter are liquids possessing an odour of garlic, and are not soluble in water. Ammonia decomposes them into mercaptans and esters of sulphocarbamic acid (p. 505) :

$$C_2H_5OCS{\cdot}SC_2H_5 + NH_3 = C_2H_5OCS{\cdot}NH_2 + C_2H_5SH.$$

Alkali alcoholates cause the production of mercaptan and alcohol, and salts of the alkyl thiocarbonic acids (p. 488) (Ber. **13,** 530) :



$$CS{<}\begin{matrix}OC_2H_5\\SC_2H_5\end{matrix} + CH_3OK + H_2O = \begin{cases}C_2H_5OH\\C_2H_5SH\end{cases} + CO{<}\begin{matrix}OCH_3\\SK\end{matrix}.$$

Ethylxanthogenic acid, C_2H_5OCSSH, is a heavy liquid, not soluble in water. It decomposes at 25° into alcohol and CS_2.

Sulphocarboxethyl disulphide, $(S{\cdot}CS{\cdot}O{\cdot}C_2H_5)_2$, m.p. 28°, is produced on adding a solution of iodine or copper salts to potassium xanthate (see above).

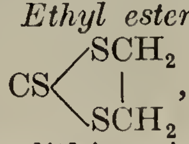
Ethyl ethylxanthogenate, $C_2H_5{\cdot}O{\cdot}CS{\cdot}S{\cdot}C_2H_5$, b.p. 200°, is a colourless oil.

Methyl xanthic ethyl ester, $CH_3OCSSC_2H_5$ (C. 1906, II. 502), b.p. 184°, and *ethyl xanthic methyl ester,* $C_2H_5{\cdot}O{\cdot}CS{\cdot}S{\cdot}CH_3$, b.p. 184°, are distinguished by their behaviour towards ammonia and sodium alcoholate (see above).

Ethylene xanthic ester, $C_2H\ (SCSOC_2H_5)_2$, is decomposed by alkalis into the cyclic trithiocarbonic ethylene ester (p. 488) and *Bender's* salt (p. 488) (Ber. **38,** 488). Ethylxanthogenyl formic ester, $C_2H_5OCS(SCOOC_2H_5)$, b.p. 133°, and ethylxanthogenyl acetic acid, $C_2H_5OCS(SCH_2COOH)$, m.p. 58°, are formed from a xanthate and chloroformic ester and chloroacetic ester respectively (J. pr. Chem. [2] **71,** 264).

5. **Trithiocarbonic acid,** $CS(SH)_2$, is precipitated by hydrochloric acid as a reddish-brown, oily liquid, from solutions of its alkali salts, which are the products of interaction between carbon disulphide and alkali sulphide. It is insoluble in water and is very unstable. CS_2 and alkaline solutions of copper form well-crystallizable double salts, CS_3CuK, $CS_3Cu(NH_4)$ (Ber. **35,** 1146). Other salts, such as $CS_3{\cdot}Ba$, see C. 1907, I. 539 : J. pr. Chem. [2] **73,** 245.

The alkali salts of the trithiocarbonic acids, reacting with the corresponding halogen compound, give rise to the following esters : *Trithiocarbonic methyl ester,* $CS(SCH_3)_2$, b.p. 204–205°. *Ethyl ester,* $CS(SC_2H_5)_2$, b.p. 240° (decomp.). *Trithiocarbonic ethylene ester,*



$CS{<}\begin{matrix}SCH_2\\|\\SCH_2\end{matrix}$, m.p. 39·5°, is converted by oxidation with dilute nitric acid into dithiocarbonic ethylene ester (p. 488) (Ann. **126,** 269).

Thiocarbonyl dithioglycollic acid, $SC(SCH_2COOH)_2$, m.p. 172°, is formed from potassium trithiocarbonate and chloroacetic acid. Oxidation converts it into *carbonyl dithioglycollic acid,* $OC(SCH_2COOH)_2$, m.p. 156° (J. pr. Chem. [2] **71,** 287).

Chlorides of the sulphocarbonic acids: thiophosgene, *thiocarbonyl chloride*, $CSCl_2$, b.p. 73°, D = 1·508, is produced when chlorine acts on carbon disulphide, and when the latter is heated with PCl_5 in closed tubes to 200°:

$$CS_2 + PCl_5 = CSCl_2 + PCl_3S.$$

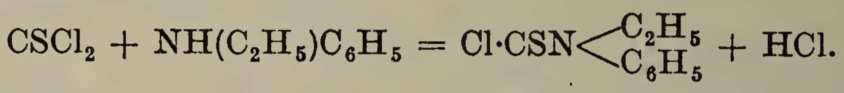
It is most readily obtained by reducing perchloromethyl mercaptan, $CSCl_4$ (below), with stannous chloride, or tin and hydrochloric acid (Ber. **20**, 2380: **21**, 102):

$$CSCl_4 + SnCl_2 = CSCl_2 + SnCl_4.$$

This is the method employed for its production in large quantities.

It is a pungent, red-coloured liquid, insoluble in water. On standing exposed to sunlight it is converted into a polymeric, crystalline compound, $C_2S_2Cl_4$ = $Cl{\cdot}CS{\cdot}S{\cdot}CCl_3$, *methyl perchlorodithioformate*, m.p. 116°, which at 180° reverts to the liquid body (Ber. **26**, R. 600). Water decomposes thiophosgene into CO_2, H_2S and 2HCl, whilst ammonia converts it into ammonium thiocyanate (p. 524).

Thiocarbonyl chloride converts secondary amines (1 molecule) into dialkyl sulphocarbamic chlorides:



$$CSCl_2 + NH(C_2H_5)C_6H_5 = Cl{\cdot}CSN\begin{smallmatrix}C_2H_5\\C_6H_5\end{smallmatrix} + HCl.$$

A second molecule of the amine produces tetraalkyl thioureas (Ber. **21**, 102).

Phosgene and thiophosgene, when acted on by alcohols and mercaptans, yield sulphur derivatives of chlorocarbonic ester.

Chlorodithiocarbonic ethyl ester, $Cl{\cdot}CSSC_2H_5$, b.p. 90°/10 mm. (Ber. **37**, 3773).

Sulphur Derivatives of Orthocarbonic Acid

Perchloromethyl mercaptan, $CCl_3{\cdot}SCl$, b.p. 147°, results from the action of chlorine on CS_2. It is a bright yellow liquid. Stannous chloride reduces it to thiophosgene. Nitric acid oxidizes it to

Trichloromethanesulphonic chloride, $CCl_3{\cdot}SO_2Cl$, m.p. 135°, b.p. 170°, which can also be made by the action of moist chlorine on CS_2. It is insoluble in water, but dissolves readily in alcohol and ether. Its odour is like that of camphor, and excites tears. Water changes the chloride to

Trichloromethanesulphonic acid, $CCl_3{\cdot}SO_3H + H_2O$, consisting of deliquescent crystals. By reduction it yields dichloromethanesulphonic acid, monochloromethanesulphonic acid, and $CH_3{\cdot}SO_3H$ (p. 176).

Dibromomethane diethyl sulphone, $CBr_2(SO_2C_2H_5)_2$, m.p. 131°, and *diethylsulphone diiodomethane*, $Cl_2(SO_2C_2H_5)_2$, m.p. 176°, are formed from methane diethyl sulphone by the action respectively of bromine water or iodine in potassium iodide, or from the potassium derivative of methane diethyl sulphone and iodine (Ber. **30**, 487).

Potassium diiodomethanedisulphonate, $CI_2(SO_3K)_2$, and *potassium iodomethanedisulphonate*, $CHI(SO_3K)_2$, are produced when potassium diazomethane disulphonate is decomposed with iodine and with hydrogen iodide. Sodium amalgam reduces both bodies to methanedisulphonic acid (p. 247).

Methanoltrisulphonic acid, $HO{\cdot}C(SO_3H)_3$. The potassium salt ($+ 1H_2O$) is obtained by heating the addition product of potassium hydrogen sulphite and potassium diazomethanedisulphonate with acids, or from the phenylhydrazone derivative of potassium methanedisulphonate (p. 247) (Ber. **29**, 2161).

Amides of Carbonic Acid

Like other dibasic acids, carbonic acid forms two amides. The monoamide, carbamic acid, $NH_2{\cdot}COOH$, does not exist in the free condition, but derivatives such as the esters, $NH_2{\cdot}COOR$, urethanes, and the acid chloride, $NH_2{\cdot}COCl$, "urea chloride," are known. The diamide, $NH_2{\cdot}CO{\cdot}NH_2$, is the well-known substance urea.

Carbamic acid, *aminoformic acid*, $H_2N{\cdot}COOH$, is not known in a free state. Its ammonium salt, $NH_2{\cdot}CO{\cdot}ONH_4$, is contained in commercial ammonium carbonate, when this is prepared by the direct union of two molecules of ammonia with one of carbon dioxide. It is a white mass which breaks up at 60° into $2NH_3$ and CO_2, which combine again upon cooling. By the absorption of water it changes into ammonium carbonate. When ammonium carbamate is heated to 130–140° in sealed tubes, water is withdrawn and urea, $CO(NH_2)_2$, formed. For other salts of carbamic acid, see J. pr. Chem. [2] **16**, 180.

The *esters* of carbamic acid are called *urethanes* ; these are obtained (1) by the action of ammonia at ordinary temperatures on carbonic esters :

$$C_2H_5O{\cdot}CO{\cdot}OC_2H_5 + NH_3 = C_2H_5O{\cdot}CO{\cdot}NH_2 + C_2H_5OH\,;$$

and (2) in the same manner from the esters of chloroformic and cyanoformic acids :

$$C_2H_5OCO{\cdot}Cl + 2NH_3 = C_2H_5OCO{\cdot}NH_2 + NH_4Cl,$$
$$C_2H_5OCO{\cdot}CN + 2NH_3 = C_2H_5OCO{\cdot}NH_2 + CN{\cdot}NH_4.$$

Also (3) by conducting cyanogen chloride into the alcohols :

$$N:CCl + 2C_2H_5{\cdot}OH = H_2N{\cdot}COOC_2H_5 + C_2H_5Cl\,;$$

(4) by the direct union of cyanic acid with the alcohols :

$$NH:CO + C_2H_5{\cdot}OH = H_2N{\cdot}COOC_2H_5.$$

When an excess of cyanic acid is employed, allophanic esters are also produced (p. 501) ;

(5) from urea chloride and the alcohols.

The urethanes are crystalline, volatile bodies, soluble in alcohol, ether and water. Sodium acts on their ethereal solution with the evolution of hydrogen ; in the case of urethane it is probable that sodium urethane, $NHNa{\cdot}COOC_2H_5$ or $NH:C(ONa)OC_2H_5$ (Ber. **23**, 2785), is produced. Alkalis decompose them into CO_2, ammonia and alcohols. They yield urea when heated with ammonia :

$$H_2NCO{\cdot}OC_2H_5 + NH_3 = H_2NCO{\cdot}NH_2 + C_2H_5OH.$$

Conversely, on heating urea or its nitrate with alcohols, the urethanes are regenerated (C. 1900, II. 997).

Carbamic esters.—*Ethyl ester,* **urethane,** $NH_2CO_2C_2H_5$, m.p. 50°, b.p. 184°, crystallizes in large plates ; *methyl ester,* m.p. 50°, b.p. 177° ; *propyl ester,* m.p. 53°, b.p. 195°.

Urethane is successfully employed as a soporific ; but is surpassed in this characteristic by higher esters, such as *methylpropylcarbinyl carbamate, Hedonal,* $NH_2COOCH(CH_3)(C_3H_7)$, m.p. 76°, b.p. 215° (C. 1900, I. 1208 : II. 997 : 1901, I. 1302) ; *allyl ester,* $NH_2COOC_3H_5$, m.p. 21°, b.p. 204°.

Acetylurethane, $CH_3CO{\cdot}NHCO_2C_2H_5$, m.p. 78°, b.p. 130°/72 mm., is obtained from acetyl chloride and urethane. Hydrogen in it can be replaced by sodium. Alkyl iodides acting on the sodium compound produce *alkylacetylurethanes* (Ber. **25**, R. 640). When heated to 150° with urea, acetyl urethane passes into acetoguanamide, or methyl dioxytriazine, and with hydrazine it yields the triazolones (Ann. **288**, 318).

Chloro- and bromo-acetylurethanes, α-bromopropionylurethanes, etc., result from the action of sodium urethane on halogen fatty-acid esters (Ber. **38**, 297).

Carbamylglycollic ester, $NH_2CO{\cdot}OCH_2CO_2C_2H_5$, m.p. 61°, and *carbamyllactic ester,* m.p. 65°, are obtained from the corresponding chloro-compounds (p. 486).

Alkyl urethanes.—The *esters of alkylcarbamic acids* are formed, like the urethanes, by (1) the action of carbonic or (2) chlorocarbonic esters on amines ; and (3) on heating *iso*cyanic esters (p. 519) with the alcohols to 100° :

$$CO:NC_2H_5 + C_2H_5OH = C_2H_5NH{\cdot}COOC_2H_5.$$

The esters of phenylcarbamic acid (phenylurethanes), $C_6H_5NH\cdot COOR$, which are obtained from phenyl *iso*cyanate and alcohols, are frequently of great value in identifying hydroxylic compounds as they are well-defined crystalline compounds. (4) By the interaction of the chlorides of alkyl ureas and the alcohols; (5) when alcohols act on acid azides (p. 324).

$$RCON_3 + C_2H_5OH = RNHCOOC_2H_5 + N_2.$$

Methylurethane, methyl carbamic ethyl ester, $CH_3\cdot HNCOOC_2H_5$, b.p. 170° (Ber. **28**, 855 : **23**, 2785), can also be prepared from sodium urethane and iodomethane.

Ethylurethane, ethyl carbamic ethyl ester, $C_2H_5HNCOOC_2H_5$, b.p. 175°.

Ethyleneurethane, $C_2H_5OCONHCH_2CH_2NHCOOC_2H_5$, m.p. 113°, is formed from ethylene diamine and $ClCO_2C_2H_5$ (Ber. **24**, 2268).

Hydroxyethyl carbamic anhydride, $\overline{OCH_2CH_2\cdot NHCO}$, m.p. 90°, is prepared from bromo-ethylamine hydrobromide, and silver or sodium carbonate (Ber. **30**, 2494).

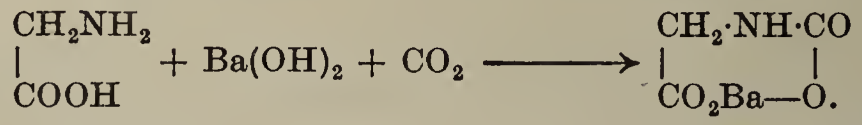
Alkylidene Urethanes and Diurethanes. *Hydroxymethylurethane*, $HOCH_2\cdot NHCO_2C_2H_5$, is prepared from glycollic acid azide and alcohol (Ber. **34**, 2795). *Methylenediurethane*, $CH_2(NHCO_2C_2H_5)_2$, m.p. 131°, is produced from urethane, formaldehyde, and a little hydrochloric acid; when heated with more acid and acetic anhydride there is formed *anhydroformaldehyde urethane*, $(CH_2:NCO_2C_2H_5)_2$, m.p. 102° (Ber. **36**, 2206).

Ethylidenediurethane, $CH_3CH(HNCOOC_2H_5)_2$, m.p. 126°, is prepared from urethane and acetaldehyde; it crystallizes in shining needles (Ber. **24**, 2268).

Chloralurethane, $CCl_3\cdot CH(OH)NHCO_2C_2H_5$, m.p. 103°, is formed from urethane and chloral. Acid anhydrides convert it into *trichloroethylideneurethane*, $CCl_3\cdot CH : NCOOC_2H_5$, m.p. 143° (Ber. **27**, 1248).

Diurethaneglyoxylic acid, $(C_2H_5OCONH)_2CHCO_2H$, m.p. 160°; *ethyl ester*, m.p. 143°, is prepared from glyoxylic ester, urethane and hydrochloric acid (C. 1906, II. 598).

Carbamic acid derivatives of the aminocarboxylic acids and peptides are of importance in the identification and synthesis of the latter bodies (p. 446). (1) Their Ca and Ba salts are obtained from the amino-acids in solutions of the alkali earths by the passage of CO_2 as more or less soluble crystalline precipitates:



$$\begin{array}{l}CH_2NH_2\\ |\\ COOH\end{array} + Ba(OH)_2 + CO_2 \longrightarrow \begin{array}{l}CH_2\cdot NH\cdot CO\\ |\qquad\qquad |\\ CO_2Ba\text{—}O.\end{array}$$

They readily decompose, re-forming the amino-acid (Ber. **39**, 397 : C. 1908, I. 1287).

(2) Esters are prepared from chloroformic esters and alkaline solutions of amino-acids or their esters.

Carbethoxyglycine, $C_2H_5O\cdot CONHCH_2COOH$, m.p. 75°; *ethyl ester*, m.p. 28°, b.p. 126°/12 mm.

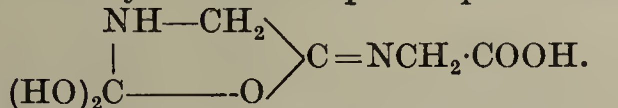
Carbomethoxyglycine, $CH_3OCONHCH_2CO_2H$, m.p. 96°; *ethyl ester*, b.p. 128°/13 mm. Thionyl chloride converts these acids into unstable *chlorides*, $ROCONHCH_2COCl$, which, on warming, give off alkyl chloride and are changed into *glycine-N-carboxylic anhydride*:

$$CH_3OCONHCH_2COCl \longrightarrow \overline{OCONHCH_2CO}.$$

The anhydride, treated with ice-cold barium hydroxide solution, yields the same compound as is obtained from the barium hydroxide solution of glycine when treated with CO_2. The anhydride on being heated loses CO_2 and polymerizes to glycine anhydride, $(NHCH_2CO)_n$ (Ber. **39**, 857). *Leucine-N-carboxylic anhydride*, $\overline{OCONHCH(C_4H_9)CO}$, m.p. 49° (Ber. **41**, 1725).

Carbethoxyalanine, $C_2H_5OCONHCH(CH_3)COOH$, m.p. 84°; *ethyl ester*, b.p. 123°/10 mm. (Ann. **340**, 127).

Carbethoxyglycylglycine ester, $C_2H_5OCO\cdot NHCH_2CONHCH_2COOC_2H_5$, m.p.

87°, is obtained from glycylglycine ester (p. 447) and $ClCO_2R$; or from carbethoxyglycine chloride (see above) and glycine ester. Hydrolysis liberates the free, dibasic *ψ-glycylglycinecarboxylic acid*, m.p. 208° (decomp.). The remarkable solubility of this compound points to its being a ring compound of the formula  It yields a *diethyl ester*, m.p. 149°, isomeric with the original carbethoxyglycylglycine ester, and a stable Ba salt, which is different from the unstable salt of the true glycylglycine acid, prepared from glycylglycine, barium hydroxide and CO_2 (Ber. **40**, 3235).

Diglycylglycinecarboxylic acid and *triglycylglycinecarboxylic acid* behave similarly (Ber. **36**, 2094).

Nitroso- and Nitro-urethanes are of interest, partly on account of their connection with the diazo- bodies (pp. 251, 458).

Nitrosocarbamic methyl ester, $NO{\cdot}NHCO_2CH_3$, m.p. 61° (Ann. **302**, 251). *Nitrosourethane*, $NO{\cdot}NHCO_2C_2H_5$, m.p. 51°, with decomposition, is formed by reduction of ammonium nitro-urethane with glacial acetic acid and zinc dust (Ann. **288**, 304). The salts of these esters probably are derived from the formula $HO{\cdot}N:NCO_2R$ (Ber. **32**, 3148 : **35**, 1148).

N-*Methylnitrosourethane*, $ON{\cdot}N(CH_3)CO_2C_2H_5$, is prepared from methyl urethane and nitrous acid. It is a liquid, which with alkalis yields diazomethane (p. 251) with the intermediate formation of $CH_3N:NOK$.

Nitrocarbamic methyl ester, $NO_2{\cdot}NHCO_2CH_3$, m.p. 88° (Ann. **302**, 249). *Nitrourethane*, $NO_2{\cdot}NHCO_2C_2H_5$, m.p. 64°, results from the action of ethyl nitrate on a cold solution of urethane in concentrated sulphuric acid. It is easily soluble in water, very easily in ether and alcohol, but with great difficulty in ligroin. It shows a strongly acid reaction, whilst its salts are neutral : *ammonium nitrourethane*, $NO_2N(NH_4)CO_2C_2H_5$; *potassium nitrourethane*, $NO_2NK{\cdot}CO_2C_2H_5$ (Ann. **288**, 267).

Nitrocarbamic acid, $NO_2{\cdot}NH{\cdot}CO_2H$, liberated from its potassium salt by sulphuric acid at 0°, decomposes into CO_2 and nitramide, NO_2NH_2, m.p. 72–85°. This is isolated by means of ether. *Potassium nitrocarbamate*, NO_2NHCO_2K, results when potassium nitrourethane is treated with potassium hydroxide in methyl alcohol. It crystallizes in fine white needles.

N-*Methylnitrourethane*, $NO_2{\cdot}N(CH_3)CO_2C_2H_5$, is formed from silver nitrourethane and iodomethane ; also from methylurethane. It is a colourless, pleasantly-smelling oil. It is decomposed by ammonia into methylnitramine (p. 201).

Urea chlorides, *carbamic acid chlorides*, are produced by the interaction of phosgene gas and ammonium chloride at 400° ; by action of $COCl_2$ on the hydrochlorides of the primary amines at 260–270°, and also on the secondary amines in benzene solution (Ber. **20**, 858 : **21**, R. 293) :

$$COCl_2 + NH_3{\cdot}HCl = ClCONH_2 + 2HCl.$$

Carbamyl chloride, *urea chloride, chloroformamide*, $Cl{\cdot}CONH_2$, m.p. 50°, b.p. 61–62°, when it dissociates into hydrochloric acid and *iso*cyanic acid, HNCO. The latter partly polymerizes to cyamelide. Urea chloride undergoes a like change on standing.

Methylcarbamyl chloride, $ClCONH{\cdot}CH_3$, m.p. 90°, b.p. 94°. *Ethylcarbamyl chloride*, $ClCONH{\cdot}C_2H_5$, b.p. 92°.

These compounds boil apparently without decomposition, but actually suffer dissociation into hydrochloric acid and *iso*cyanic esters, which reunite on cooling :

$$CONCH_3 + HCl = Cl{\cdot}CONH{\cdot}CH_3.$$

Dimethylcarbamyl chloride, $Cl{\cdot}CON(CH_3)_2$, b.p. 167° C., yields tetramethyloxamide by the action of sodium.

Diethylcarbamyl chloride, $Cl{\cdot}CON(C_2H_5)_2$, b.p. 190–195°, is obtained from diethyl oxamic acid by means of PCl_5.

Reactions.—(1) The urea chlorides are decomposed by water into CO_2 and ammonium chloride. (2) They yield urethanes with alcohols.

(3) With amides they form alkylureas :

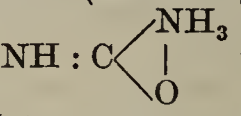
$$H_2NCOCl + 2C_2H_5{\cdot}NH_2 = H_2NCONHC_2H_5 + C_2H_5NH_2{\cdot}HCl.$$

(4) With benzene and phenol ethers in the presence of $AlCl_3$ they yield aromatic acid amides :

$$ClCO{\cdot}NH_2 + C_6H_6 \xrightarrow{AlCl_3} C_6H_5CONH_2 + HCl.$$

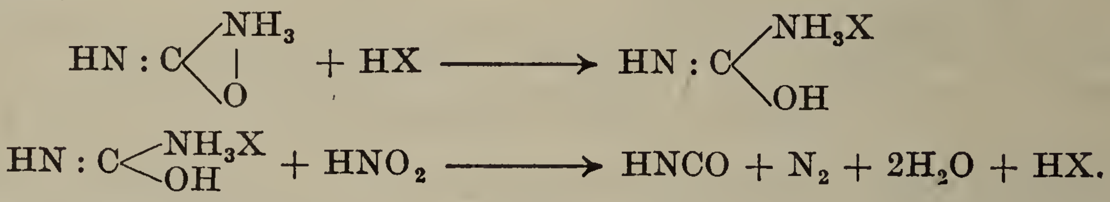
Carbamide, urea, $CO{<}\begin{smallmatrix}NH_2\\NH_2\end{smallmatrix}$, m.p. 132–133°, was discovered by v. Rouelle in urine in 1773, and was first synthesized from ammonium *iso*cyanate by Wöhler in 1828 (Pogg. Ann. (1825) 3, 177 : (1828) 12, 253). This brilliant discovery showed that organic as well as inorganic elements could be built up artificially from their elements.

Urea occurs in various animal fluids, chiefly in the urine of mammals, and can be separated as nitrate from concentrated urine on the addition of nitric acid. It is present in small quantities in the urine of birds and reptiles. A full-grown man voids upon an average diet about 30 grams of urea daily. The formation of this substance is due to the decomposition of proteins.

Constitution of Urea.—Urea is usually represented by the "carbamide" formula, $NH_2{\cdot}CO{\cdot}NH_2$, but Werner (Chemistry of Urea, London, 1923) has put forward the alternative formula  to represent the "static" formula of urea and $NH_2{\cdot}C(=NH){\cdot}OH$ to represent it in its reactive form.

It is impossible to reproduce briefly the arguments which have been adduced in support of this formulation, but the following examples may show some of the difficulties inherent in the carbamide formula. The methods of formation of urea (3) and (4) on p. 495 which are usually represented as examples of ordinary amide formation are interpreted otherwise by Werner. They do not, in actual fact, take place like the formation of an amide. For instance, the formation of urea from ethyl carbonate and ammonia requires heating in a sealed tube, whereas the formation of acetamide from ethyl acetate takes place readily at ordinary temperature, while from carbonyl chloride and ammonia, urea is, indeed, formed, but only slowly and in 30–40 per cent. yield, accompanied by large amounts of the by-products biuret, ammelide and cyanuric acid, whereas the reaction between acetyl chloride and ammonia is a very violent one, the acetamide produced being accompanied by inappreciable amounts of by-product. These results, and the actual findings in other syntheses of urea, can be explained by assuming the intermediate formation of cyanic acid, HNCO, which then combines with ammonia to form urea, as in Wöhler's synthesis.

Similarly, the breakdown of urea by nitrous acid is usually represented as in (3) (p. 496), as a simple decomposition into nitrogen and water, but in actual fact the reaction takes place differently. It does not occur in the presence of pure nitrous acid, but a strong mineral acid is required to convert the urea into a salt before reaction can occur, the volume of nitrogen evolved is not that corresponding to the urea calculated according to equation (3) and the ratio $CO_2 : N_2$ is not 1 : 2. Further, cyanic acid can be isolated in large quantity as its silver salt from the products of reaction. These changes are represented by Werner as follows :



For further consideration of these and other reactions of urea, Werner's book should be consulted.

It should be noted, however, that the cyclic formula is very difficult to visualize on the basis of the modern electronic theory, as nitrogen does not appear capable of more than four covalent links.

Formation.—Urea is obtained by the following methods:

(1) By evaporating the aqueous solution of ammonium *iso*cyanate, when an atomic transposition occurs (*Wöhler*):

$$CO : N{\cdot}NH_4 \longrightarrow CO(NH_2)_2$$

Mixed aqueous solutions of potassium cyanate and ammonium sulphate (in equivalent quantities) are evaporated; on cooling, potassium sulphate crystallizes out and is filtered off, the filtrate being evaporated to dryness, and the urea extracted by means of hot alcohol. This is also a reversible process. On heating a $N/10$ urea solution for some time to 100°, 4% to 5% of the urea will be changed to ammonium cyanate (Ber. **29**, R. 829: C. 1903, I. 139).

(2) When a solution of carbon monoxide in ammoniacal cuprous chloride solution is heated, copper is precipitated and urea is formed (C. 1899, I. 422):

$$CO + 2NH_3 + Cu_2Cl_2 = CO(NH_2)_2 + 2HCl + 2Cu.$$

It is also formed by the methods in general use in the preparation of acid amides: (3) by the action of ammonia (*a*) on carbamic esters or urethanes, (*b*) on dialkyl or diphenyl carbonic esters (Ber. **17,** 1826), and (*c*) on chloroformic esters. The bodies mentioned under *b* and *c* first change to carbamic esters:

$$\begin{aligned}NH_2{\cdot}CO_2C_2H_5 + NH_3 &= NH_2CONH_2 + C_2H_5OH\\ CO(OC_2H_5)_2 + 2NH_3 &= NH_2CONH_2 + 2C_2H_5OH\\ CO(OC_6H_5)_2 + 2NH_3 &= NH_2CONH_2 + 2C_6H_5OH \text{ (method of preparation)}\\ ClCO_2C_2H_5 + 3NH_3 &= NH_2CONH_2 + C_2H_5OH + NH_4Cl.\end{aligned}$$

(4) By the action of ammonia on phosgene and urea chloride:

$$\begin{aligned}COCl_2 + 4NH_3 &= CO(NH_2)_2 + 2NH_4Cl\\ ClCONH_2 + 3NH_3 &= CO(NH_2)_2 + NH_4Cl.\end{aligned}$$

(5) By heating ammonium carbamate or thiocarbamate to 130–140°.

Urea is manufactured on the large scale for use as manure by heating carbon dioxide and ammonia together under high pressure, best in nickel autoclaves (D.R.PP. 294,793: 390,848).

(6) It can also be obtained by the reaction between carbon oxysulphide and ammonia (Z. anorg. Chem. **191**, 246).

(7) By the action of potassium permanganate on thiocarbamide, $CS(NH_2)_2$.

(8) By the hydrolysis of cyanamide with small amounts of acid:

$$CN{\cdot}NH_2 + H_2O = CO(NH_2)_2.$$

(9) Urea is formed when guanidine is boiled with dilute sulphuric acid or barium hydroxide solution:

$$NH : C(NH_2)_2 + H_2O = CO(NH_2)_2 + NH_3.$$

Urea crystallizes in long, rhombic prisms or needles, which have a cooling taste, like that of potassium nitrate. It can be easily obtained pure by one recrystallization from amyl alcohol (Ber. **26**, 2443). It dissolves in one part of cold water and in five parts of alcohol, and it is almost insoluble in ether.

Reactions.—(1) By heating to high temperatures, urea decomposes into ammonia, *biuret* (p. 502), *ammelide* (p. 531), *cyanuric acid* (p. 520) and *cyanuryltriurea* (p. 522).

(2) When heated above 100° with water, or when heated with acids or alkalis, urea is decomposed into carbon dioxide and ammonia. The same decomposition takes place under the influence of micro-organisms when urine decomposes.

An enzyme, *urease*, which occurs in considerable quantity in Soya-bean or Jack-bean, is also capable of hydrolysing urea to ammonia and carbon dioxide. The hydrolysis of urea by urease, forms a valuable method for the quantitative estimation of urea. After the enzyme has acted, the solution is made alkaline and the ammonia formed distilled off or aspirated into standard acid, and the excess acid titrated with standard alkali, using methyl orange or other suitable indicator.

(3) Urea, like other amides, is decomposed by nitrous acid, with the formation of nitrogen :

$$CO(NH_2)_2 + 2HNO_2 \longrightarrow CO_2 + 2N_2 + 3H_2O.$$

(4) Hypobromites decompose urea into nitrogen, carbon dioxide and water : in the presence of benzaldehyde, sodium hypochlorite yields with urea the hydrazone or carboxyhydrazone of benzaldehyde, a Hofmann reaction (see p. 191) taking place.

$$NH_2{\cdot}CO{\cdot}NH_2 + NaOCl + C_6H_5{\cdot}CHO \longrightarrow C_6H_5CH : N{\cdot}NH{\cdot}COOH + NaCl + H_2O.$$

Salts : Urea, like glycocoll, forms crystalline compounds with acids, bases and salts. Although it contains two NH_2 groups it combines with but one equivalent of acid.

Urea nitrate, $CO(NH_2)_2{\cdot}HNO_3$, forms leaf-like crystals, which are difficultly soluble in nitric acid. The *oxalate*, $[CO(NH_2)_2]_2(CO_2H)_2$, consists of thin leaflets, which are soluble in water.

Urea forms a large number of compounds with neutral salts, of which the compound with *sodium chloride*, $CO(NH_2)_2$, NaCl, H_2O, may be cited as an example.

Urea forms the principal end-product of protein metabolism among the mammals and batrachians, and on this account its estimation becomes of importance. Birds and reptiles, on the other hand, excrete most of their nitrogen in the form of ammonium urate.

Estimation of Urea.—The method usually used for the estimation of nitrogen in excretions is that of Kjeldahl (p. 9), though of course this includes all nitrogenous products, and is not specific for urea. The methods mostly used at the present time are of three main types :

(*a*) The reaction with hypobromite, followed by measurement of the nitrogen evolved. This is a rapid, but not very accurate method.

(*b*) The urea is hydrolysed to ammonia and carbon dioxide by some urease preparation, and the ammonia produced titrated against standard acid (see (2) above). In dealing with small amounts of urea, such as those occurring in blood, the ammonia produced is frequently estimated colorimetrically by means of the colour it produces with *Nessler's reagent* (alkaline mercury potassium iodide).

(*c*) Urea forms a very insoluble compound when treated with a methyl alcohol solution of xanthydrol. This reaction is sometimes used for the estimation of urea, the dixanthydrylurea being weighed (Compt. rend. **159**, 367), estimated colorimetrically by means of the yellow colour it produces with concentrated sulphuric acid (Biochem. J. **22**, 711) or estimated by oxidation with standard permanganate solution (J. Biol. Chem. **79**, 211) or better by potassium dichromate (J. Biol. Chem. **82**, 693).

The details of some of these methods are given in the textbooks of physiological chemistry, such as Hawk and Bergeim or Cole.

Alkyl ureas are produced according to the same reactions which yield urea (1) when primary or secondary amines act on *iso*cyanic esters or *iso*cyanic acid:

$$CO:NH + NH_2\cdot C_2H_5 = \underset{\text{Ethylurea.}}{NH_2CONHC_2H_5}$$

$$CO:NC_2H_5 + NH(C_2H_5)_2 = \underset{\text{Triethylurea.}}{N(C_2H_5)_2CONHC_2H_5}.$$

Alkylureas are formed, also, when *iso*cyanic esters are heated with water. CO_2 and amines are produced (p. 190); the latter unite with a further molecule of *iso*cyanate:

$$CO:NC_2H_5 \xrightarrow{H_2O} CO_2 + NH_2C_2H_5 \xrightarrow{CONC_2H_5} CO(NHC_2H_5)_2.$$

(2) They are also obtained by the action of carbamyl chloride and alkyl-carbamyl chlorides on ammonia, and primary and secondary amines (p. 187), as well as by the action of phosgene on the latter.

(3) By the action of alkali hydroxides on the ureides, the urea derivatives containing acid radicals:

$$\underset{\text{Methylacetylurea.}}{CH_3\cdot NHCONH\cdot COCH_3} + KOH = \underset{\text{Methylurea.}}{CH_3\cdot NHCONH_2} + CH_3CO_2K.$$

(4) By desulphurizing the alkyl thioureas with an alcoholic silver nitrate solution (Ber. **28**, R. 915).

Alkylureas resemble urea itself so far as properties and reactions are concerned. They generally form salts with one equivalent of acid. They are crystalline salts, with the exception of those containing four alkyl groups. On heating those with one alkyl group, cyanic acid (or cyanuric acid) and an amine are produced. The higher alkylated members can be distilled without decomposition. Boiling alkalis convert them all into CO_2 and amines:

$$CH_3NH\cdot CONH_2 + H_2O = CO_2 + NH_3 + NH_2\cdot CH_3.$$

Methylurea,, $CH_3\cdot NHCONH_2$, m.p. 102°, results on heating methyl acetourea (from acetamide by the action of bromine and potassium hydroxide) with potassium hydroxide.

Ethylurea, $C_2H_5\cdot NHCONH_2$, m.p. 92°.

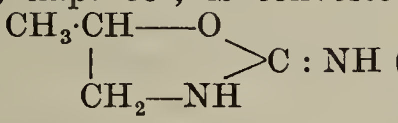
sym-*Diethylurea*, $CO(NH\cdot C_2H_5)_2$, m.p. 112°, b.p. 263°.

unsym.-*Diethylurea*, $(C_2H_5)_2NCONH_2$, m.p. 70°.

Triethylurea, $(C_2H_5)_2NCONHC_2H_5$, m.p. 63°, b.p. 223°.

Tetraethylurea, b.p. 210–215°, has an odour resembling that of peppermint.

Tetrapropylurea, b.p. 258° (Ber. **28**, R. 155).

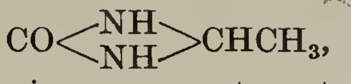
Allylurea, $C_3H_5NHCONH_2$, m.p. 85°, is converted by hydrogen bromide into propylene-ψ-urea (p. 503),  $\begin{array}{l}CH_3\cdot CH—O\\ |\qquad\quad >C:NH\\ CH_2—NH\end{array}$ (Ber. **22**, 2990: C. 1898, II. 766).

Diallyl urea, sinapoline, $CO(NH\cdot C_3H_5)_2$, m.p. 100°, is formed when allyl*iso*cyanate is heated with water, or by heating mustard oil with water and lead oxide. Diallyl thiourea is first formed, but the lead oxide desulphurizes it (p. 509).

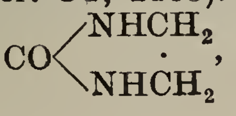
Carbamido-ethyl alcohol, $HOCH_2CH_2\cdot NHCONH_2$, m.p. 95°, is obtained from hydroxyethylamine *iso*cyanate (Ber. **28**, R. 1010).

Cyclic Alkylene Urea Derivatives.

The ureas and aldehydes combine at the ordinary temperature, with loss of water, to yield the following compounds:

Methyleneurea,  $CO{<}\begin{smallmatrix}NH\\NH\end{smallmatrix}{>}CH_2$, consists of white, granular crystals (Ber. **29**, 2751: C. 1897, II. 736), and *ethylideneurea*,  $CO{<}\begin{smallmatrix}NH\\NH\end{smallmatrix}{>}CHCH_3$, m.p. 154°, are decomposed, by boiling with water, into their component parts.

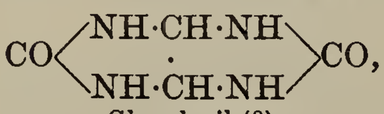
When HCl gas is passed into a mixture of acetone and urea, there is formed *triacetone diurea*, $(CH_3)_2C[NHCON:C(CH_3)_2]_2 + 3H_2O$, m.p. 265–268° with decomposition (Ber. **34**, 2185).

Ethyleneurea,  $CO{<}\begin{array}{l}NHCH_2\\ \quad\cdot\\ NHCH_2\end{array}$, m.p. 131°, is produced on heating ethyl carbonate with ethylenediamine at 180°. It is also formed, together with hydantoin (p. 499), when parabanic acid or oxalylurea is electrolytically reduced (Ber. **34**, 3286). Nitric acid produces *ethylene dinitrourea.* The union of ethylene diamine and cyanic acid, however, gives rise to *ethylenediurea*, $NH_2CONH \cdot CH_2 \cdot CH_2NHCONH_2$.

Trimethyleneurea, $CH_2 < \begin{matrix} CH_2NH \\ CH_2NH \end{matrix} > CO$, m.p. 260°, is obtained from ethyl carbonate and trimethylenediamine ; or by the electrolytic reduction of barbituric acid and related compounds (see Malonyl urea). Similarly, the reduction of methyl uracil (p. 629) produces *methyltrimethyleneurea*, $CH_2 < \begin{matrix} CH(CH_3)NH \\ CH_2 \text{———} NH \end{matrix} > CO$, m.p. 201° (Ber. **33**, 3378 : **34**, 3286).

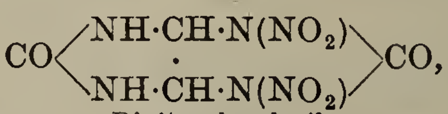
Very little is known relative to the action of urea on dialdehydes, aldehydeketones, and diketones.

Acetylenediurea, glycoluril, $C_3H_6N_4O_2$, is obtained from glyoxal and urea, as well as by the reduction of allantoin (Ber. **19**, 2477). Nitric acid converts it into *dinitroglycoluril* (decomposes at 217°), and when boiled with water passes into *glycolureine*, $C_3H_6N_2O_3$, isomeric with hydantoic acid.



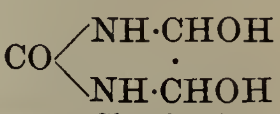
$$CO < \begin{matrix} NH \cdot CH \cdot NH \\ \cdot \\ NH \cdot CH \cdot NH \end{matrix} > CO,$$

Glycoluril (?).



$$CO < \begin{matrix} NH \cdot CH \cdot N(NO_2) \\ \cdot \\ NH \cdot CH \cdot N(NO_2) \end{matrix} > CO,$$

Dinitroglycoluril.



$$CO < \begin{matrix} NH \cdot CHOH \\ \cdot \\ NH \cdot CHOH \end{matrix}$$

Glycolureine.

Consult Ber. **26**, R. 291, for the action of urea on acetyl acetone.

Nitrosoureas are formed when nitrites act on the nitrates or sulphates of ureas which contain an alkyl group in the amido group :

Nitroso-methylurea, $NH_2 \cdot CO \cdot N(NO)CH_3$. *Nitroso*-sym.-*diethylurea*, $NH(C_2H_5)CON(NO)C_2H_5$, m.p. 5°, is a yellow oil at the ordinary temperature. The reduction of these compounds gives rise to the *semicarbazides* (p. 503).

Nitrourea, $NO_2 \cdot NHCONH_2$, is produced when urea nitrate is introduced into concentrated sulphuric acid. It forms a white, crystalline powder when recrystallized from water. It melts at 159° with decomposition. It is immediately decomposed by sodium hydroxide solution (Ber. **59**, 1870).

unsym.-*Nitro-ethylurea*, $NO_2 \cdot NHCONH \cdot C_2H_5$, m.p. 130–131°.

Derivatives of Urea with Organic Acid Radicals : Ureides

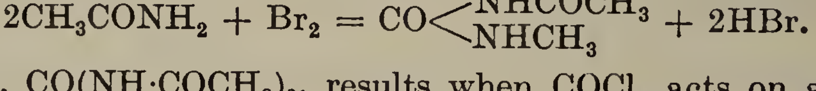
The urea derivatives of the monobasic carboxylic acids are obtained by the action of acid chlorides or acid anhydrides on urea. By this procedure, however, it is possible to introduce but one radical. The compounds are solids ; they decompose when heat is applied to them, and do not form salts with acids. Alkalis cause them to separate into their components.

Formylurea, $NH_2CONH \cdot CHO$, m.p. 167° (Ber. **29**, 2046).

Acetylurea, $NH_2CONH \cdot COCH_3$, m.p. 218° (Ann. **229**, 30 : C. 1898, II. 181), is slightly soluble in cold water and alcohol. It forms long, silky needles. (Consult Ber. **28**, R. 63, for the metal derivatives of formyl and acetyl urea.) Heat breaks it up into acetamide and *iso*cyanuric acid. *Chloroacetylurea*, $H_2NCONH \cdot COCH_2Cl$, decomposes about 160°. *Bromoacetylurea*, $NH_2CONH \cdot COCH_2Br$, dissolves with difficulty in water. When heated with ammonia it changes to hydantoin.

The ureides of the *dialkylacetic acids*, such as $(C_2H_5)_2CHCONHCONH_2$, m.p. 207°, are also obtained from dialkylmalonic acids (p. 545) and urea by means of phosphorus chloride, etc. (C. 1903, II. 813).

Acetylmethylurea, $CH_3 \cdot NHCONH \cdot COCH_3$, m.p. 180°, is obtained from methylurea upon digesting it with acetic anhydride ; and by the action of bromine and potassium hydroxide on acetamide (p. 323) :



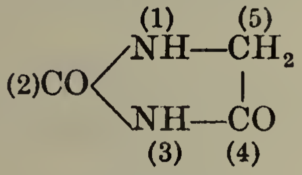
$$2CH_3CONH_2 + Br_2 = CO < \begin{matrix} NHCOCH_3 \\ NHCH_3 \end{matrix} + 2HBr.$$

Diacetylurea, $CO(NH \cdot COCH_3)_2$, results when $COCl_2$ acts on acetamide, and sublimes in the form of needles without decomposition.

Various remedies employed in the treatment of sleeping sickness are derived from complex compounds of urea with naphthylaminesulphonic acids and aminobenzoic acids (*e.g. Germanin*) (Z. angew. Chem. **39**, 680 : J.C.S. **1927**, 3068).

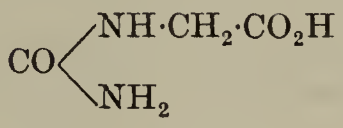
Ureides of Hydroxy-acids.—Open-chain and cyclic ureides are known, particularly those of α-hydroxy-acids, such as glycollic, lactic, and α-hydroxy*iso*butyric acids. The open-chain ureides are obtained from the closed-chain members by severing a lactam-union by means of alkalis or alkali earths :

(I)



Hydantoin.
Cyclic ureide of
glycollic acid.

(II)



Hydantoic acid.
Open-chain ureide
of glycollic acid.

Hydantoin, *glycollylurea,* $C_3H_4O_2N_2$ (Formula (I) above), m.p. 216°, possesses the same series of C and N atoms as the glyoxalines or iminazoles (p. 399), but the ring is less stable than the glyoxaline ring.

It is prepared (1) by reduction, by means of hot hydriodic acid, of allantoin (*q.v.*) and alloxan (*q.v.*), both important oxidation products of urea. Also, by electrolytic reduction of parabanic acid (oxalylurea) (Ber. **34**, 3286).

(2) It is synthetically produced from bromoacetylurea (see above) by heating it with alcoholic ammonia, whereby it gives up hydrobromic acid.

(3) By the action of urea on dihydroxytartaric acid (Ann. **254**, 258). (4) By evaporating a solution of hydantoic ester (below) with hydrochloric acid (method of preparation).

Chlorine produces *dichlorohydantoin,* $C_3H_2Cl_2O_2N_2$, m.p. 121°. Bromine gives rise to a body which easily changes into parabanic acid (see above) (Ann. **327**, 355 : **348**, 85). Concentrated nitric acid produces 1-*nitrohydantoin,* $CO{\cdot}N(NO_2)CH_2CO{\cdot}NH$, m.p. 170°, which on being boiled with water evolves CO_2 and is converted into nitroamino-acetamide (Ber. **22**, R. 58). Only the 1-NH-group is substituted on nitration. 1-*Acetylhydantoin,* $CON(COCH_3)CH_2CONH$, m.p. 144°, is prepared from hydantoin and acetic anhydride ; it cannot be nitrated (Ann. **327**, 353).

When boiled with barium hydroxide solution hydantoin is converted into glycoluric acid or hydantoic acid :

$$CO{\cdot}NH{\cdot}CH_2{\cdot}CO{\cdot}NH + H_2O = H_2N{\cdot}CONH{\cdot}CH_2{\cdot}COOH.$$

Hydantoic acid, *glycoluric acid,* $NH_2CONH{\cdot}CH_2CO_2H$, was originally obtained from uric acid derivatives (allantoin, glycouril, hydantoin), but may be synthesized by heating urea with glycocoll to 120°, by boiling it with barium hydroxide solution (Ber. **39**, 2954), or by digesting glycocoll sulphate with potassium *iso*cyanate, similarly to the preparation of urea (p. 494).

Hydantoic acid is very soluble in hot water and alcohol. When heated with hydriodic acid it yields CO_2, NH_3 and glycocoll ; *ethyl* *ester*, m.p. 135°, is easily obtained by the addition of potassium cyanate to glycocoll ester hydrochloride (Ber. **33**, 3418). It is also formed from glycine ester and sodium methane (Ber. **38**, 305).

Hydantoin Homologues.—For nomenclature, see the hydantoin formula (p. 499) and also Ann. **327**, 355. Hydantoin, alkyl iodides, and alkali give rise to 3-*alkylhydantoins*, in which the NH-group between the two CO-groups is alkylated (see also Ber. **22**, 685 : **25**, R. 327).

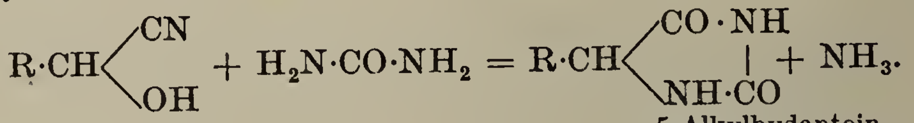
The 1-*alkylhydantoins* are formed when urea is fused together with mono-alkylic glycocolls.

3-*Methylhydantoin*, $CONHCH_2CONCH_3$, m.p. 184°, is formed from silver hydantoin and iodomethane. Nitric acid converts it into 1-*nitro*-3-*methylhydantoin*, m.p. 168° (Ann. **361**, 69). 3-*Ethylhydantoin*, m.p. 102°.

1-*Methylhydantoin*, $CO{\cdot}N(CH_3){\cdot}CH_2{\cdot}CO{\cdot}NH$, m.p. 157°, was first obtained from creatinine, and is also formed when sarcosine (p. 441) is heated with urea; or by heating the sarcosine with cyanogen chloride (Ber. **15**, 2111).

1-*Ethylhydantoin*, m.p. 100°, sublimes readily.

The **5-Alkylhydantoins** may be synthesized by heating the cyanohydrins of the aldehydes and ketones (p. 433) with urea (see Ber. **21**, 2320):



$$R{\cdot}CH\begin{cases}CN\\OH\end{cases} + H_2N{\cdot}CO{\cdot}NH_2 = R{\cdot}CH\begin{cases}CO{\cdot}NH\\NH{\cdot}CO\end{cases} + NH_3.$$

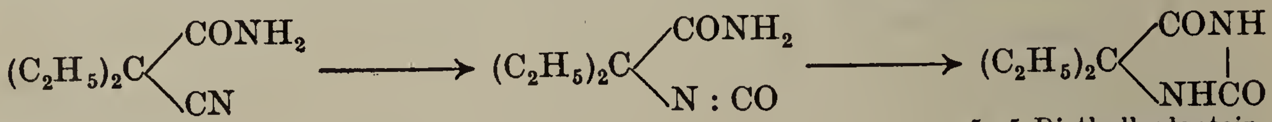
5-Alkylhydantoin.

5-*Methylhydantoin*, α-*lactylurea*, $CO{\cdot}NH{\cdot}CH(CH_3)CO{\cdot}NH + H_2O$, m.p. 140–145° (anhydrous) is formed, together with alanine from aldehyde ammonia by the action of potassium *iso*cyanate containing potassium cyanate. Also, by the action of warm hydrochloric acid on α-*lacturamic ester* (ethyl-α-carbamidopropionate), $NH_2CONHCH(CH_3)CO_2C_2H_5$, m.p. 94°, the product of alanine ester hydrochloride and potassium cyanate. Lactyl urea when boiled with barium hydroxide solution yields *lacturamic acid*, m.p. 155°. With 2 molecules of bromine it is converted into *bromopyruveide*, $BrCH : CNHCONHCO$, m.p. 242°, which unites the excess of lactyl urea to form *pyruvic ureide*, $C_8H_8N_4O_6$.

1 : 5-*Dimethylhydantoin*, m.p. 221°, and 1 : 5-*methylethylhydantoin*, m.p. 85°, are prepared from *N*-methylalanine and *N*-ethylalanine respectively, potassium cyanate, and hydrochloric acid. 5-*Ethylhydantoin*, m.p. 118°, is obtained from α-aminobutyric acid (Ann. **348**, 50). 5-iso*Butylhydantoin*, m.p. 210°. iso*Butylhydantoic acid* is prepared from leucine, urea, and barium hydroxide solution; it is employed in the identification of leucine on account of its slight solubility (p. 444) (Ber. **39**, 2953).

5 : 5-*Dimethylhydantoin*, α-iso*butyrylurea*, $CONH{\cdot}C(CH_3)_2CONH$, m.p. 175°, is produced from acetone, hydrocyanic acid, and cyanic acid (Ann. **164**, 264); also from pinacolyl sulphourea (p. 509) and $KMnO_4$, α-*carbamido*iso*butyric acid*, $NH_2CO{\cdot}NHC(CH_3)_2COOH$, m.p. 155–160°; both these substances are ureides of α-hydroxy*iso*butyric acid.

5 : 5-*Dialkylhydantoins*, *e.g.* 5 : 5-*diethylhydantoin*, m.p. 165°, can also be prepared from cyanacetamide, by converting the latter into diethyl cyanacetamide, and treating this with bromine and alkali solution (Gazzetta, **26**, I. 197):

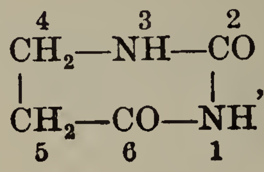


$$(C_2H_5)_2C\begin{cases}CONH_2\\CN\end{cases} \longrightarrow (C_2H_5)_2C\begin{cases}CONH_2\\N : CO\end{cases} \longrightarrow (C_2H_5)_2C\begin{cases}CONH\\NHCO\end{cases}$$

Diethyl cyanacetamide.

5 : 5-Diethylhydantoin.

Hydrouracil, β-*lactylurea*, $C_4H_6N_2O_2$ = , m.p. 275°, is



$$\begin{array}{ccc} ^{4} & ^{3} & ^{2} \\ CH_2\text{—} & NH & \text{—}CO \\ | & & | \\ CH_2\text{—} & CO & \text{—}NH \\ _{5} & _{6} & _{1} \end{array}$$

obtained similarly to diethylhydantoin, by treating succinamide with bromine and alkali, through an unstable intermediate product, $\begin{array}{l}CH_2\cdot CO\cdot NH_2\\ | \\ CH_2N : CO\end{array}$. It has been obtained by several other methods. It results, together with trimethylene urea, from the electrolytic reduction of barbituric acid (malonyl urea), of dialuric acid (tartronyl urea), and of uramil (aminomalonyl urea) (Ber. **34**, 3286). Further, by heating acrylic acid with urea at 210–220°, and from β-aminopropionic acid and cyanic acid (Ber. **38**, 635).

5-*Methylhydrouracil*, $(CH_3)C_4H_5N_2O_2$, m.p. 265°, and 4-*methylhydrouracil*, m.p. 220°, are similarly prepared by heating urea with methyl acrylic acid and crotonic acid. 4-Methylhydrouracil is also produced from β-aminobutyric acid and urea, and from β-aminobutyric ester and cyanic acid.

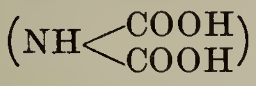
Bromine in glacial acetic acid yields bromo-derivatives of hydrouracil, which easily give up HBr, and are converted into uracils (Ber. **34**, 3751, 4129 : **38**, 636).

The uracils or ureides of β-aldehydo- and keto-carboxylic acids, together with those of glyoxylic, oxalic, malonic, tartronic, and mesoxalic acids, will be considered later in connection with uric acid.

Di- and Tri-carboxylamide Derivatives. *Ureides of Carbonic Acid.*—Free dicarbaminic or imidodicarbonic acid and the free tricarbamic acids or nitrogen tricarboxylic acids are as unstable as free carbaminic acid itself (p. 490) ; but the esters, amides, and nitriles of these acids are known. They sustain the same relation to carbamic acid that diglycollamic acid bears to glycocoll :

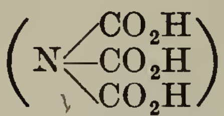
(NH_2COOH)

Carbamic acid.



$\left(NH\begin{array}{l}\diagup COOH\\ \diagdown COOH\end{array}\right)$

Dicarbamidic acid.
Iminodicarboxylic acid.



$\left(N\begin{array}{l}\diagup CO_2H\\ — CO_2H\\ \diagdown CO_2H\end{array}\right)$

Tricarbamidic acid.
Nitrilotricarboxylic acid.

Dicarbamidic ester, *iminodicarboxylic ester*, $NH(CO_2C_2H_5)_2$, m.p. 50°, b.p. 215°, results when $ClCO_2C_2H_5$ acts on 2 molecules of sodium urethane ; from nitrogen tricarboxylic ester by decomposition with alkali ; and from carboxethyl *iso*cyanate (p. 520) and alcohol. The ester yields a *sodium salt*, $NaN(CO_2R)_2$, more readily than urethane and acetyl urethane (p. 520) (Ber. **36**, 736 : **39**, 686).

Allophanic acid, $NH_2CONH\cdot CO_2H$, is not known in a free state. A *disodium salt* of this acid, $NH_2CON(Na)CO_2Na$, appears to be formed when a benzene solution of urethane is boiled in the presence of sodium (Ber. **35**, 779). Its esters are formed (1) when chloroformic esters (1 mol.) act on urea (2 mols.) (Ber. **29**, R. 589) ; (2) by passing cyanic acid vapours into anhydrous alcohols (p. 518). At first carbamic acid esters are produced ; these combine with a second molecule of cyanic acid and yield allophanic esters (Ber. **22**, 1572) :

$$HNCO + NH_2\cdot CO_2C_2H_5 = NH_2CONH\cdot CO_2C_2H_5.$$

From carbamic esters or urethanes (3) by the action of carbamyl chloride (Ber. **21**, 293) ; (4) carbonyl chloride (Ber. **19**, 2344) or (5) with thionyl chloride (Ber. **26**, 2172) :

$$2NH_2CO_2C_2H_5 + SOCl_2 = NH_2CONH\cdot CO_2C_2H_5 + HCl + SO_2 + C_2H_5Cl.$$

For the formation of allophanic esters by decomposition of α-hydroxy-acid azides see Ber. **34**, 2794. Nitrogen tricarboxylic ester and also carbethoxyl *iso*cyanate, $C_2H_5O\cdot CO\cdot NCO$ (pp. 502, 520) with ammonia, yield allophanic ester (Ber. **39**, 686).

Allophanic ethyl ester, $NH_2CONHCO_2C_2H_5$, m.p. 191° ; *propyl ester*, m.p. 155° ; *amyl ester*, m.p. 162°.

The allophanic esters dissolve with difficulty in water, and, when heated, split up into alcohol, ammonia, and cyanuric acid. The allophanates are obtained from them by means of the alkalis or barium hydroxide solution. They show an alkaline reaction and are decomposed by carbon dioxide. On attempting to free the acid by means of mineral acids, it at once breaks up into CO_2 and urea.

Cyanocarbamic acid, *cyanamide carboxylic acid*, $CN\cdot NHCO_2H$, is the corresponding nitrile acid of allophanic acid. Its salts are formed by the addition of CO_2 to salts of cyanamide (Ann. **331**, 270) :

$$2CN\cdot NHNa + CO_2 = NC\cdot N : C(ONa)_2 + CN\cdot NH_2.$$

The *esters* of this acid result by the action of alcoholic potassium hydroxide on esters of cyanamidedicarboxylic acid.

Biuret, *allophanamide,* $NH_2 \cdot CO \cdot NH \cdot CO \cdot NH_2 + H_2O$, m.p. 190° (anhydrous) is formed on heating the allophanic esters with ammonia to 100°, or urea to 150–160°:

$$NH_2CONH_2 = NH_2 \cdot CO \cdot NH \cdot CO \cdot NH_2 + NH_3.$$

It is readily soluble in alcohol and water, and decomposes, when heated, into NH_3 and cyanuric acid. Heated in a current of HCl, biuret decomposes into NH_3, CO_2, cyanuric acid, urea, and guanidine. The aqueous solution, containing KOH, is coloured a violet red by copper sulphate. (*The biuret reaction:* C. 1898, I. 375; Ber. **35**, 1105: Ann. **352**, 73.)

Nitrobiuret, $NH_2CO \cdot NH \cdot CO \cdot NH \cdot NO_2$, m.p. 105° (decomp.), is converted by hydrochloric acid and zinc dust into *aminobiuret,* the hydrochloride of which when boiled with water gives urazole (p. 505), and when treated with sodium nitrite yields *allophanic azide,* $NH_2CO \cdot NHCON_3$ (Ann. **303**, 93).

Imidodioximidocarbonic acid, $NH\left(C \lessdot \substack{NOH \\ OH}\right)_2$, m.p. 65–70°, is prepared from $Hg(CH_3)_2$ and nitrogen peroxide (C. 1898, II. 1015).

Carbamyl cyanide, cyanourea, $NH_2CONH \cdot CN$, the half-nitrile of biuret, is formed, like urea from guanidine, from cyanoguanidine or dicyandiamide (p. 515), by the action of barium hydroxide solution; when digested with mineral acids it yields *biuret* (Ber. **8**, 708). (See Ber. **25**, 820, for alkyl cyanoureas.)

Carbonyldiurethane, $CO(NHCOOC_2H_5)_2$, m.p. 107°, is prepared from urethane (C. 1897, II. 25) and urea by the action of phosgene at 100°; also from carboxyethyl *iso*cyanate (p. 520) and water.

Carbonyldiurea, $CO(NHCONH_2)_2$, m.p. 231°, is also produced from urethane (C. 1897, II. 25), and urea with phosgene at 100°. When heated it passes directly into NH_3 and cyanuric acid (p. 520) (Ber. **29**, R. 589).

Carbonyldimethylurea, $CO(NHCONH \cdot CH_3)_2$, m.p. 197°, similarly to the above, yields *N*-methyl cyanuric acid, on being heated (Ber. **30**, 2616).

Tricarbamidic ester, *nitrogen tricarboxylic ester,* $N(COOC_2H_5)_3$, b.p. 147° /12 mm., is prepared from sodium urethane or sodium imidodicarboxylic ester and chlorocarbonic ester. It is a colourless and odourless oil, scarcely soluble in water.

For the action of alkali and of P_2O_5, see next paragraph.

Cyanimidodicarboxylic ester, nitrogen tricarboxylic di-ester nitrile, $N \vdots C - N = (CO_2C_2H_5)_2$, results from the interaction of sodium cyanamide, CNNHNa, and chlorocarbonic ester. Alkali splits off a carboxethyl group; P_2O_5 causes the liberation of CO_2 and $2C_2H_4$, leaving carboxethyl *iso*cyanate (J. pr. Chem. [2] **16**, 146: Ber. **39**, 686).

Derivatives of Imidocarbonic Acid.—The *pseudo*-forms, imidocarbonic acid and *pseudo*-urea, correspond with carbamic acid and urea:

$NH_2 \cdot COOH$	$NH : C(OH)_2$	$CO(NH_2)_2$	$NH : C \lessdot \substack{NH_2 \\ OH}$
Carbamic acid.	Imidocarbonic acid.	Urea.	ψ-Urea.

These modifications are not known in a free state, but many derivatives may be referred to them.

Imidocarbonic ester, $HN : C(OC_2H_5)_2$, b.p. 62°/36 mm., is produced by reducing chloroimidocarbonic ester (Ber. **19**, 862, 2650); from di-imidooxalic ester (p. 541) by the action of alcoholic sodium ethoxide (Ber. **28**, R. 760), and from cyanogen chloride (p. 522) by the same reagent. At 200° it breaks down into alcohol and cyanuric ester (Ber. **28**, 2466).

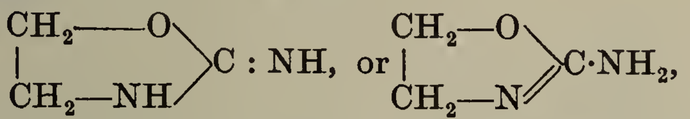
Chloroimidocarbonic ethyl ester, $ClN : C(OC_2H_5)_2$, m.p. 39°, and the *methyl ester,* m.p. 20°, are produced in the action of esters of hypochlorous acid (p. 169) on a concentrated potassium cyanide solution. They are solids, with a peculiar penetrating odour, and distil with decomposition. Alkalis have little effect upon them, whilst acids break them up quite easily, forming ammonia, esters of carbonic acid and nitrogen chloride.

Bromoimidocarbonic ethyl ester, $BrN : C(OC_2H_5)_2$, m.p. 43°, results when bromine acts on imidocarbonic ester (Ber. **28**, 2470).

Ethylimidochlorocarbonic ester, $C_2H_5N : CCl(OC_2H_5)$, b.p. 126°, is formed by the union of ethyl *iso*cyanide (p. 293) with ethyl hypochlorite (Ber. **28**, R. 760).

Derivatives of ψ- or *iso*-Urea.—*Methyl-ψ-urea*, $NH : C<^{OCH_3}_{NH_2}$, m.p. 45°, b.p. 82°/9 mm., and *ethyl-ψ-urea*, $HN : C(OC_2H_5)NH_2$, m.p. 42°, b.p. 96°/15 mm., are formed as *hydrochlorides* by the action of alcohols on equimolecular quantities of cyanamide and hydrochloric acid : $N \vdots CNH_2 \xrightarrow[CH_3OH]{HCl} HN : C(NH_2)(OCH_3)\cdot HCl$. The hydrochlorides are decomposed when heated in aqueous solution into chloromethane and urea. A similar decomposition occurs with the numerous derivatives of these substances. These ψ-urea ethers can also be considered as being alkoxy-formamidines or aminoformimido-ethers. Chloroformic ester produces O-*methylallophanic ester*, $CH_3OC(NH_2)NCO_2C_2H_5$, m.p. 5° ; *iso*cyanic acid, O-*methylbiuret*, $CH_3OC(NH_2) : NCONH_2$, m.p. 118° ; acetoacetic ester, *methyluracil* (p. 472) ; oxalic ester, *O*-methyl parabanic acid. Hydrochloric acid causes these substances to decompose into chloromethane and allophanic ester, biuret, methyl uracil, and parabanic acid. *Acetylmethyl-ψ-urea*, $CH_3O\cdot C(NH_2)$-$NCOCH_3$, m.p. 58° (C. 1904, II. 29 : Ber. **38**, 2243).

Ethylene-ψ-urea, 2-*aminooxazoline*,



is produced by the action of bromoethylamine hydrobromide on potassium cyanate or from sodium cyanamide and ethylene chlorohydrin. It forms very hygroscopic crystals (Ber. **31**, 2832 : Ann. **442**, 130).

Propylene-ψ-urea, $C_3H_6 : CON_2H_2$, results from bromopropylamine hydrochloride and potassium cyanate ; as well as from allylurea, by a molecular rearrangement induced by hydrobromic acid (Ber. **22**, 2991 : C. 1898, II. 760).

Hydrazine-, Azine-, and Azido-derivatives of Carbonic Acid

Hydrazinecarboxylic acid, $NH_2NHCOOH$ or NH_3NHCOO, is precipitated when CO_2 is passed into a cold aqueous solution of hydrazine, in the form of a white powder. It decomposes at 90° into CO_2 and the *hydrazine salt* of hydrazinecarboxylic acid, $NH_2NHCO_2\cdot N_2H_5$, m.p. 70° (appr.), b.p. 75°/23 mm., (appr.). *Ethyl ester*, $NH_2NHCO_2C_2H_5$, b.p. 92°/13 mm., is produced from nitrourethane (p. 493) by reduction with zinc and acetic acid ; also by the decomposition of nitrogen tricarboxylic ester with hydrazine.

Benzalhydrazine carboxylic ester, m.p. 135° (Ann. **288**, 293 : Ber. **36**, 745 : **37**, 4523 : C. 1905, I. 1222).

Sodium benzalhydrazine carbonate, $C_6H_5CH : NNHCO_2Na$, is prepared from urea, NaClO, and benzaldehyde (*cf.* p. 496).

Azidocarbonic methyl ester, $N_3CO_2CH_3$, b.p. 102°, is obtained from chlorocarbonic methyl ester and ammonium nitrate ; as well as from hydrazine carboxylic acid and nitrous acid (J. pr. Chem. [2] **52**, 461 : Ber. **36**, 2057).

Semicarbazide, *carbamic hydrazide*, $\overset{4}{NH_2}\cdot\overset{3}{CO}\cdot\overset{2}{NH}\cdot\overset{1}{NH_2}$, is an important reagent used for the identification of ketonic compounds, as it frequently yields sparingly soluble, crystalline condensation products, *semicarbazones*, with them.

It is formed (1) by heating urea and hydrazine hydrate to 100° (J. pr. Chem. [2] **52**, 465) ; (2) from hydrazine sulphate and potassium cyanide ; (3) from aminoguanidine (Ber. **27**, 31, 56) ; (4) from nitrourea (Ann. **288**, 311).

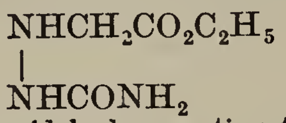
Acetaldehyde semicarbazone, $NH_2CONH\cdot N : CHCH_3$, m.p. 162°, is prepared from aldehyde-ammonia and semicarbazide hydrochloride (Ann. **303**, 79) : *benzaldehyde semicarbazone*, $NH_2CONHN{=}CHC_6H_5$, m.p. 214°. *Acetone semicarbazone*, $NH_2CONHN : C(CH_3)_2$, m.p. 187°, passes into dimethyl ketazine (p. 269) (Ber. **29**, 611).

Acetoacetic ester semicarbazone, $NH_2CONHN : C(CH_3)CH_2CO_2C_2H_5$, m.p. 129° (Ann. **283**, 18), readily passes into a lactazam. Semicarbazide condenses with benzil to 1 : 2-diphenyl oxytriazine (Vol. III).

Alkyl semicarbazides are obtained (1) by reduction of the nitroso-alkylureas (p. 498); (2) from alkylhydrazines by means of *iso*cyanic acid or its esters, whereby the secondary NH-group receives the carbamide residue. The alkyl semicarbazides only react easily with the aldehydes when the hydrazine NH_2-group is free (C. 1901, I. 1170 : Ber. **37**, 2318).

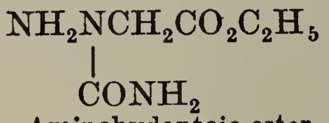
2-*Methylsemicarbazide*, $NH_2N(CH_3)$, $CONH_2$, m.p. 113°. 2 : 4-*Methylethylsemicarbazide*, $NH_2N(CH_3)CONHC_2H_5$, is an oil. 1 : 2-*Dimethylsemicarbazide* $CH_3NHN(CH_3)CONH_2$, m.p. 116° (Ber. **39**, 3263).

Carbamidohydrazoacetic ester, m.p. 122°, and *aminohydantoic ester*, m.p. 70–74°, are prepared from hydrazinoacetic ester (p. 452) and cyanic acid (Ber. **31**, 167). 1-*Aminohydantoin*, m.p. 244°, is formed by loss of alcohol from aminohydantoic ester:



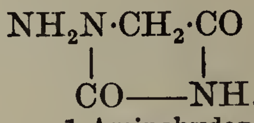
$$\begin{array}{l}NHCH_2CO_2C_2H_5\\ |\\ NHCONH_2\end{array}$$

Carbamidohydrazoacetic ester.



$$\begin{array}{c}NH_2NCH_2CO_2C_2H_5\\ |\\ CONH_2\end{array}$$

Aminohydantoic ester.



$$\begin{array}{l}NH_2N{\cdot}CH_2{\cdot}CO\\ \;\;|\qquad\quad |\\ CO\text{——}NH.\end{array}$$

1-Aminohydantoin.

Carbohydrazide, $NH_2NH{\cdot}CO{\cdot}NHNH_2$, m.p. 152–153°, is obtained from carbonic ester and hydrazine hydrate on heating to 100° (J. pr. Chem. [2] **52**, 469). *Dibenzal carbohydrazide*, $CO(NHN{=}CHC_6H_5)_2$, m.p. 198°.

Imidodicarboxylic hydrazide, $NH(CONHNH_2)$, m.p. 200° with decomposition, is obtained from nitrogen tricarboxylic ester and hydrazine. It is easily decomposed into N_2H_4 and urazole (see below) (Ber. **36**, 744).

Hydrazodicarbonic ester, hydrazinedicarboxylic ester, $C_2H_5OCONHNHCOO{\cdot}C_2H_5$, m.p. 130°, b.p. with decomposition about 250°, and is prepared from hydrazine and $Cl{\cdot}CO_2C_2H_5$ (Ber. **27**, 773 : J. pr. Chem. [2] **52**, 476).

Hydrazodicarbonamide, hydrazoformamide, $NH_2CO{\cdot}NHNH{\cdot}CONH_2$, m.p. 245° (decomp.). It is obtained from potassium cyanate and salts of hydrazine. It also results upon heating semicarbazide (Ber. **27**, 57), and from *azodicarbonamide* (see below) by reduction. It yields the latter upon oxidation (Ann. **271**, 127 : Ber. **26**, 405). NaOCl partially decomposes it into hydrazoic acid, carbon dioxide, and ammonia (J. pr. Chem. [2] **76**, 433).

Azodicarboxylic acid, *azoformic acid*, $CO_2HN{=}NCO_2H$, is prepared from azodicarboxylic amide and concentrated potassium hydroxide solution, in the form of yellow needles. Its potassium salt deflagrates at 100°. It readily decomposes in aqueous solution into CO_2, potassium carbonate, hydrazine, and nitrogen. It is not possible to obtain from it the still unknown diimide $NH{=}NH$. *Diethyl ester*, b.p. 106°/13 mm., is prepared from the hydrazo-ester (see above) and nitric acid. It is an orange-yellow oil.

The **azodicarboxylic esters,** $RO{\cdot}CO{\cdot}N : N{\cdot}COOR$, are very reactive compounds which readily form addition compounds at the N : N double bond:

$$R{\cdot}H + EtOCO{\cdot}N : N{\cdot}COOEt \longrightarrow EtO{\cdot}CO{\cdot}NH{\cdot}NR{\cdot}COOEt$$

Addition compounds have been obtained by this reaction with alcohols and mercaptans (Ann. **437**, 309) : with amines and enolic compounds (Ann. **429**, 1), with aromatic hydrocarbons (Ber. **57**, 106). With azoimide alkoxytetrazoles and iminodicarboxylic esters are formed (Ber. **57**, 1656).

Azodicarboxylic amide, azoformamide, $NH_2CON{=}NCONH_2$, is formed (1) by the oxidation of hydrazodicarboxylic amide with chromic acid, and (2) from azodicarboxylic diamidine, $NH_2C(NH)N : NC(NH)NH_2$ (p. 516). It is an orange-red powder.

Carbamic acid azide, *azidocarbonic amide*, N_3CONH_2, m.p. 97°, is prepared from semicarbazide and nitrous acid; and by the combination of hydrazoic and cyanic acids. Silver nitrate decomposes it into silver cyanate and silver azide; when heated with water it is split up into N_3H, NH_3, and CO_2. Hydrogen sulphide reduces the azide to urea (Ann. **314**, 339). Hydrocyanic acid unites with it to form urea azocyanide, carbamidocyanotriazene, $NH_2CONHN : NCN$.

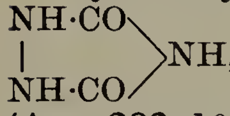
Carbodiazide, carbazide, nitrogen carbonyl, $CO(N_3)_2$, is produced from carbohydrazide and nitrous acid:

$$CO(NHNH_2{\cdot}HCl)_2 + 2KNO_2 = CO(N_3)_2 + 2NaCl + 4H_2O.$$

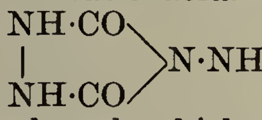
It forms spear-like, very volatile crystals, of a penetrating and stupefying odour, recalling that of phosgene (p. 486) and hydrazoic acid. It is explosive. The aqueous solution decomposes into CO_2 and $2N_3H$ (Ber. **27**, 2684 : J. pr. Chem. [2] **52**, 482).

Hydrazidicarbohydrazide, $NH_2 \cdot NH \cdot CO \cdot NH \cdot NH \cdot CO \cdot NH \cdot NH_2$, m.p. 196°, is obtained, together with aminourazole, by the action of hydrazine hydrate on hydrazidicarboxylic ester (Ber. **43**, 2468). With nitrous acid it yields :

Hydrazidicarbonazide, $N_3 \cdot CO \cdot NH \cdot NH \cdot CO \cdot N_3$, white needles, m.p. 146° (150°) (Ber. **47**, 728).



Cyclic Hydrazine Derivatives of Urea.—**Urazole**, *hydrazodicarbonimide*, $\begin{matrix} NH \cdot CO \\ | \\ NH \cdot CO \end{matrix} \Big> NH$, m.p. 244°, is formed on heating hydrazodicarbonamide to 200° (Ann. **283**, 16), or from urea and hydrazine sulphate heated to 120° (Ber. **27**, 409). It is a strong, monobasic acid. For its alkylation, see C. 1898, I. 38.

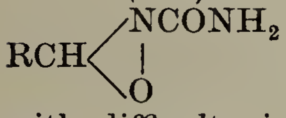


Aminourazole, $\begin{matrix} NH \cdot CO \\ | \\ NH \cdot CO \end{matrix} \Big> N \cdot NH_2$, m.p. 270°, is probably the same as diurea or bis-hydrazinocarboxyl, which is obtained from hydrazo-dicarbonic ester and hydrazine hydrate at 100° (Ber. **46**, 2094).

Methenylcarbohydrazide, $CO {<}{\begin{matrix} NH - N \\ NH \cdot NH \end{matrix}}{>} CH$, m.p. 181°, is produced on heating carbohydrazide with orthoformic ester to 100° (J. pr. Chem. [2] **52**, 475).

Hydroxylamine Derivatives of Carbonic Acid.—*Hydroxyurethane*, $HO \cdot NHCO_2C_2H_5$, or $HON : C {<}{\begin{matrix} OC_2H_5 \\ OH \end{matrix}}$, is a colourless liquid. It is produced when an hydroxylamine solution acts on chlorocarbonic ester (Ber. **27**, 1254).

Hydroxyurea, *carbamidoxime*, $NH_2CONH \cdot OH$, m.p. 128°, is obtained from hydroxylamine nitrate and potassium *iso*cyanate, together with a (? stereo-) isomeric body iso*hydroxyurea*, m.p. 70–72° (decomp.), which when heated in alcoholic solution changes into the ordinary hydroxyl-urea.



Methylhydroxyurea, $CH_3NHCO \cdot NHOH$, m.p. 127° (decomp.), and *ethylhydroxyurea*, m.p. 129° (decomp.), are formed from methyl and ethyl *iso*cyanate and hydroxylamine (C. 1902, I. 31). *Dimethyl-nitroso-hydroxy-urea*, $(CH_3)_2NCO \cdot N(NO)OH$ (Ber. **30**, 2356). *Aldehyde-derivative* of carbamidoxime, $RCH {<}{\begin{matrix} NCONH_2 \\ | \\ O \end{matrix}}$ (C. 1908, I. 948) dissolves readily in water and alcohol, but with difficulty in ether.

Sulphur Derivatives of Carbamic Acid and Urea

The compounds to be discussed in this section include thiocarbamic acid, $NH_2 \cdot COSH$, which forms two series of esters, the *S*-esters, $NH_2 \cdot CO \cdot SR$ (thiocarbamic esters), and the *O*-esters, $NH_2 \cdot CS \cdot OR$ (sulphocarbamic esters), dithiocarbamic acid, $NH_2 \cdot CSSH$, and thiocarbamide, $NH_2 \cdot CS \cdot NH_2$ or $NH : C(SH) \cdot NH_2$.

Thiocarbamic acid, $NH_2 \cdot COSH$, is not known in the free state. Its *ammonium salt*, $NH_3 \cdot CO \cdot SNH_4$, is prepared by leading COS into alcoholic ammonia (Ann. **285**, 173). It is a colourless, crystalline mass, which is unstable on exposure to the air. When heated to 130° it breaks up into hydrogen sulphide and urea.

Alkylamines and COS yield alkyl ammonium salts of alkyl carbamine-thiolic acids, such as *ethyl carbamine-thiolic acid*, $C_2H_5 \cdot NH \cdot CO \cdot SH$, and iso*butyl carbamine-thiolic acid*, $C_4H_9NH \cdot COSH$. The mercury salts of these two acids decompose when heated into *iso*cyanic esters and dialkyl ureas (*cf.* p. 497) (Ann. **359**, 202).

***S*-Esters.**—*Thiol-carbamic methyl ester*, NH_2COSCH_3, or $HO \cdot C(: NH) \cdot SCH_3$, m.p. 95°, and *ethyl ester*, m.p. 108°, both result from the action of ammonia (1) on dithiocarbonic ester (p. 488), (2) on chlorocarbonthiolic ester ; (3) by the passage of HCl into a solution of potassium or alkyl thiocyanate (Ber. **14**, 1083) in alcohol, when the *O*-ester is also formed (J. pr. Chem. [2] **16**, 358). These are crystalline compounds which dissolve with difficulty in water.

Thiol-carbethylamine ethyl ester, $C_2H_5NH \cdot COSC_2H_5$, b.p. 204–208°. It results from the union of ethyl *iso*cyanate with ethyl mercaptan.

O-**Esters.**—The esters of sulphocarbamic acid—*thiourethanes*, the *xanthogenamides*—are formed when alcoholic ammonia acts on the xanthic esters (p. 489):

$$C_2H_5S{\cdot}CSOC_2H_5 + NH_3 = NH_2{\cdot}CSOC_2H_5 + C_2H_5SH.$$

The O-*ethyl ester*, m.p. 38°, and O-*methyl ester*, m.p. 43°, are both slightly soluble in water. Both esters decompose into mercaptans, cyanic acid and cyanuric acid when heated. Alcoholic alkalis decompose them into alcohols and thiocyanates.

The **alkylthiocarbamic esters** are obtained when the mustard oils are heated to 110° with anhydrous alcohols:

$$CS : N{\cdot}C_2H_5 + C_2H_5{\cdot}OH = C_2H_5NH{\cdot}CS{\cdot}OC_2H_5.$$

They are liquids with an odour like that of leeks, boil without decomposition and with acid or alkali break up into alcohols, CO_2, H_2S, and alkylamines, and can easily be transformed by halogen alkyls into the isomeric thiolcarbamic esters (above) (C. 1899, II. 618).

Ethylthiocarbamic ethyl ester, $C_2H_5{\cdot}NHCSOC_2H_5$, m.p. 46°, b.p. 206°. *Allylthiocarbamic ethyl ester*, $C_3H_5{\cdot}NHCSOC_2H_5$, b.p. 210–215°, is prepared from allyl mustard oil. *Acetylthiocarbamic methyl ester*, $CH_3CO{\cdot}NHCS(OCH_3)$, m.p. 80°, is prepared from thiocarbamic ester and acetic anhydride; or from lead thiocyanate, acetyl chloride, and methyl alcohol. It is converted by iodomethane into the isomeric S-*methyl acetylthiolcarbamate*, $CH_3CO{\cdot}NHCOSCH_3$, m.p. 146° (C. 1900, II. 853).

Ethers are also known derived from the tautomeric form, $NH : C(OH){\cdot}SH$, of thiocarbamic acid.

Dithiocarbamic acid, $NH_2{\cdot}CSSH$ or $NH{=}C(SH)_2$, is obtained as a red oil upon decomposing its ammonium salt with dilute sulphuric acid. It readily breaks down into thiocyanic acid, $HS{\cdot}NC$, and hydrogen sulphide. Water decomposes it into cyanic acid and $2H_2S$. Its *ammonium salt*, $NH_2{\cdot}CSSNH_4$, is formed when alcoholic ammonia acts on carbon disulphide. It consists of yellow needles or prisms.

Alkyl Dithiocarbamic Acids, *Dithiocarbalkylaminic Acids.*—The amino-salts of these compounds are formed by heating together carbon disulphide and primary or secondary amines in alcoholic solution:

$$CS_2 + 2C_2H_5NH_2 = C_2H_5NH{\cdot}CSSNH_3C_2H_5.$$

When the amine salts of ethyl dithiocarbamic acid are heated to 110° dialkylated thioureas are formed (p. 509):

$$C_2H_5NHCS{\cdot}SH,NH_2C_2H_5 = C_2H_5NHCSNHC_2H_5 + H_2S.$$

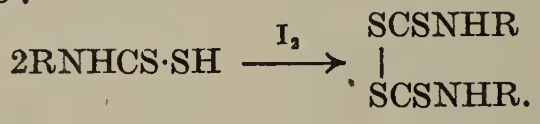
If the salts formed with *primary amines* are heated in aqueous solution with metallic salts such as $AgNO_3$, $FeCl_3$, or $HgCl_2$, salts of ethyldithiocarbamic acid are precipitated:

$$C_2H_5NHCSS(NH_3C_2H_5) \xrightarrow{AgNO_3} C_2H_5NHCSSAg + HNO_3,H_2NC_2H_5,$$

which, when boiled with water, yield mustard oils or *iso*thiocyanic esters (p. 526).

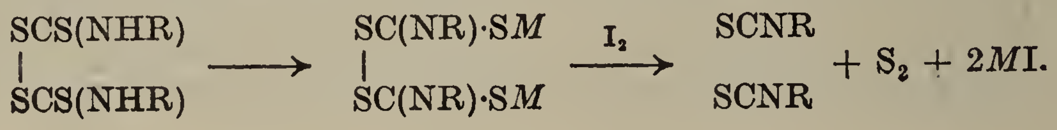
The *secondary amine* salts of dithiocarbamic acid give no mustard oil (Ber. **8**, 107).

Oxidation with iodine changes the mono- and di-alkyl dithiocarbamic acids into *thiuram disulphides*:



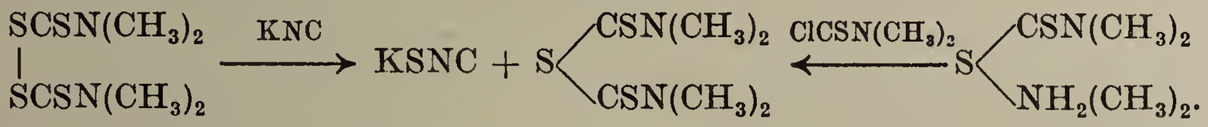
$$2RNHCS{\cdot}SH \xrightarrow{I_2} \begin{array}{l} SCSNHR \\ | \\ SCSNHR. \end{array}$$

These disulphides, when possessing hydrogen atoms available for the reaction are decomposed by heat partly into mustard oils, S and H_2S, and partly into dialkylthioureas, S, and CS_2. Sodium alcoholate converts them into salts of the isomeric *iso*thiuram disulphide. The latter are converted directly into mustard oil and sulphur by repeated treatment with iodine (Ber. **35**, 817).



$$\begin{array}{l} SCS(NHR) \\ | \\ SCS(NHR) \end{array} \longrightarrow \begin{array}{l} SC(NR){\cdot}SM \\ | \\ SC(NR){\cdot}SM \end{array} \xrightarrow{I_2} \begin{array}{l} SCNR \\ \\ SCNR \end{array} + S_2 + 2MI.$$

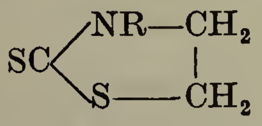
If alkyl or acyl halides are employed instead of iodine, the decomposition results in the formation of mustard oil, dialkyl disulphides, or diacyl disulphides (pp. 173, 320) (Ber. **36**, 2259). Tetraalkyl thiuram disulphides and potassium cyanide yield the yellow coloured *thiuram monosulphide* and potassium thiocyanate. These are also obtained from dithiocarbamic salts with dithiocarbamic acid chlorides (see below (Ber. **36**, 2275)):

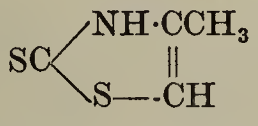


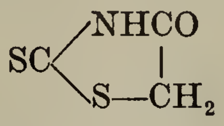
Dithiourethanes, *dithiocarbamic esters,* are obtained by several methods (Ber. **35**, 3368: C. 1903, I. 139). They are readily prepared (1) from ammonium dithiocarbamate (below) and alkyl iodides:

$$NH_2CSS{\cdot}NH_4 \xrightarrow{CH_3I} NH_2CSSCH_3\ ;\ (CH_3)_2NCS_2NH_2(CH_3)_2 \xrightarrow{CH_3I} (CH_3)_2NCS_2CH_3.$$

It must be noticed, however, that alkylene dihalides, α-halogen ketones, and α-halogen fatty esters convert the dithiocarbamates easily into cyclic thiazole derivatives:







(2) from chlorodithiocarbonic esters (p. 490) and amines:

$$C_2H_5SCSCl + NH(C_3H_7)_2 \longrightarrow C_2H_5SCSN(C_3H_7)_2$$

(3) from thiocyanic esters and H_2S:

$$C_2H_5SC\vdots N + H_2S \longrightarrow C_2H_5SCSNH_2.$$

The dithiocarbodialkylamine acid esters are stable, whilst the simpler derivatives easily decompose into mercaptans and mustard oils or thiocyanic acid.

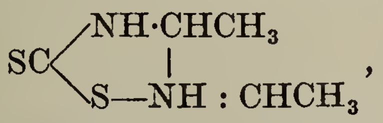
Dithiocarbamic methyl ester, $NH_2CS_2CH_3$, m.p. 41°; *ethyl ester,* m.p. 42°; iso*propyl ester,* m.p. 97°; *allyl ester,* m.p. 32°.

Methyldithiocarbamic methyl ester, $CH_3NHCS_2CH_3$, b.p. 156°/20 mm. *Dimethyldithiocarbamic methyl ester,* $(CH_3)_2NCS_2CH_3$, m.p. 47°. Excess of alkyl iodide converts the dithio- and alkyl dithio-carbamic esters into the hydroiodides of imidodithiocarbonic esters, $HN{\cdot}C(SCH_3){\cdot}RN : C(SC_2H_5)_2$, which, on hydrolysis, yield dithiocarbonic esters (p. 488).

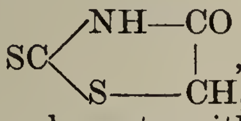
Acetyldithiourethanes, $CH_3CONHCS_2R$, are produced from acylation of dithiourethane, and from mustard oils by means of thioacetic acid (p. 320). They are converted by sodium alcoholate and iodo-alkyls into acetyl imidodithiocarbonic ester, $CH_3CONC(SR)_2$ (C. 1901, II. 764): 1903, I. 446).

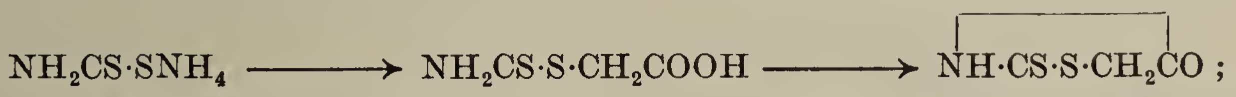
Dialkylthiocarbamyl chlorides, NR_2CSCl, are formed from thiophosgene and amines (Ber. **36**, 2274).

Cyclic Derivatives of Dithiocarbamic Acid.—*Carbothialdine,*



is obtained by heating ammonium dithiocarbamate with aldehyde; and by mixing CS_2 with alcoholic aldehyde-ammonia. It forms large shining crystals. Isomeric with this is *dimethylformocarbothialdine,* $CS_2(NCH_3)_2(CH_2)_2$, which is prepared from CS_2 and formaldehyde-methylimide. Iodomethane breaks it down into *methylimidodithiocarbonicdimethyl ester,* $CH_3N : C(SCH_3)_2$ (see above) (C. 1896, II. 478).

Rhodanic acid, , m.p. 169°, with decomposition, is prepared from ammonium dithiocarbamate with salts or esters of chloro- or thio-acetic acid;



$$NH_2CS{\cdot}SNH_4 \longrightarrow NH_2CS{\cdot}S{\cdot}CH_2COOH \longrightarrow NH{\cdot}CS{\cdot}S{\cdot}CH_2CO\ ;$$

the homologous α-halogen fatty acids behave similarly. Mustard oils (p. 526) and thioacetic acid form *n*-alkyl rhodanic acids. Rhodanic acid condenses with aromatic aldehydes, eliminating water and forming dyes: ArCH : (C_3S_2NOH) (C. 1903, I. 446 : II. 836 : 1906, I. 1436 : Ber. **39**, 3068). These condensation products are valuable synthetic reagents (*e.g.* for aminoacids, Helv. Chim. Acta. **5**, 610 : **6**, 458).

Thiocarbamide, *thiourea, sulphourea,* $CS{<}^{NH_2}_{NH_2}$, or $NH:C{<}^{NH_2}_{SH}$, m.p. 172°, is obtained (as first observed by *Reynolds* in 1869—Ann. **150**, 224) by heating ammonium thiocyanate to 170–180° (Ann. **179**, 113), when a transposition analogous to that occurring in the formation of urea takes place (p. 494). This synthesis, however, does not proceed with ease, and is never complete, because at 160–170° thiocarbamide is again changed to ammonium thiocyanate:

$$CSN{\cdot}NH_4 \rightleftarrows CS(NH_2)_2.$$

Sulphourea is also produced by the action of hydrogen sulphide (in presence of a little ammonia) or of ammonium thiocyanate on cyanamide (Ber. **8**, 26):

$$CNNH_2 + SH_2 = CS(NH_2)_2.$$

Thiocarbamide crystallizes in thick, rhombic prisms, which dissolve easily in water and alcohol, but with difficulty in ether; they possess a bitter taste and have a neutral reaction.

Reactions.—(1) When sulphocarbamide is heated with water to 140° it reverts to ammonium thiocyanate. (2) If boiled with alkalis, hydrochloric acid or sulphuric acid, it decomposes according to the equation:

$$CSN_2H_4 + 2H_2O = CO_2 + 2NH_3 + H_2S.$$

(3) Silver, mercury, or lead oxides and water convert it, at ordinary temperatures, into cyanamide, CN_2H_2; and on boiling into dicyandiamide (p. 515). (4) $KMnO_4$ changes it, in cold aqueous solution, into urea. (5) In nitric acid solution, or by means of H_2O_2 in oxalic acid solution, salts of a disulphide, $[NH_2{\cdot}C(:NH){\cdot}S—]_2$, not known in a free state, are produced (Ber. **24**, R. 71). (See Ber. **25**, R. 676, upon the condensation of thiourea with aldehyde-ammonias.) Sulphourea condenses with α-chloroaldehydes and α-chloroketones to aminothiazoles (Vol. III). It yields aromatic glyoxaline derivatives (Vol. III) when heated with benzoin.

Constitution.—The behaviour of thiourea when oxidized in acid solution, and certain other reactions, rather support the formula $NH:C{<}^{NH_2}_{SH}$ instead of the diamide formula (*cf.* J. pr. Chem. [2] **47**, 135).

Werner has suggested, on the grounds of the high melting point and solubility in water of thiourea, the internal salt formula $NH:C\begin{matrix}\diagup NH_3\\ \mid\\ \diagdown S\end{matrix}$. On the ground of the equivalence of the atoms combined with the C atom, Lecher has suggested the dipole formula $S^-{\cdot}C\left.\begin{matrix}\diagup\cdot NH_2\\ \diagdown\cdot NH_2\end{matrix}\right\}^+$, which also represents the hybrid nature of thiourea. (Discussion on constitution, see Ann. **438**, 169.)

Salts.—Thiocarbamide forms salts with one equivalent of acid, to which the name *thiuronium salts* and the constitution $HS{\cdot}C\left.\begin{matrix}\diagup\cdot NH_2\\ \diagdown\cdot NH_2\end{matrix}\right\}^+X^-$ has been ascribed. (See also Ann. **445**, 35.)

The *nitrate*, CSN_2H_4, NHO_3, forms large crystals. *Hydrochloride*, see C. 1902,

I. 113. *Gold chloride* and *platinum chloride* precipitate red *double salts* from the concentrated solution. *Silver nitrate* precipitates the complex, $B.AgNO_3$ (Ber. **24**, 3956 : **25**, 583). These numerous heavy metal compounds may be regarded as organic molecular compounds (see Pfeiffer, Org. Molekülverb., 1922, p. 130).

Alkylthiocarbamides, in which the alkyl groups are linked to nitrogen, are produced—

(1) On heating the mustard oils with primary and secondary amine bases (*A. W. Hofmann*, Ber. **1**, 27):

$$NH_3 + CS : N{\cdot}C_2H_5 = \underset{\text{Ethylthiocarbamide.}}{NH_2{\cdot}CS{\cdot}NHC_2H_5.}$$

$$NH_2{\cdot}C_2H_5 + CS : N{\cdot}C_2H_5 = \underset{\textit{sym.}\text{-Diethylthiocarbamide.}}{NHC_2H_5CSNHC_2H_5.}$$

$$NH(C_2H_5)_2 + CS : N{\cdot}C_2H_5 = \underset{\text{Triethylthiocarbamide.}}{N(C_2H_5)_2CSNHC_2H_5.}$$

(2) By heating the amine salts of the alkyl dithiocarbamic acids (Ber. **1**, 25) (p. 506):

$$C_2H_5NHCS{\cdot}SNH_3C_2H_5 = C_2H_5NH{\cdot}CS{\cdot}NHC_2H_5 + H_2S.$$

(3) By heating the corresponding aminothiocyanates (Ber. **24**, 2724 : **26**, 2497).

Ethylthiocarbamide, $NH_2CSNH{\cdot}C_2H_5$, m.p. 113°, dissolves readily in water and alcohol. sym.-*Diethylthiocarbamide*, $CS(NH{\cdot}C_2H_5)_2$, m.p. 77°. *Triethylthiocarbamide*, m.p. 26°, b.p. 205°.

Methylthiourea, m.p. 119°. sym.-*Dimethylthiourea*, m.p. 61° (Ber. **24**, 2729 ; **28**, R. 424). unsym.-*Dimethylthiourea*, $NH_2CSN(CH_3)_2$, m.p. 159° (Ber. **26**, 2505). *Tetramethylthiourea*, m.p. 78° (Ber. **43**, 1857).

Propylthiourea, see Ber. **23**, 286 : **26**, R. 87.

Allylthiocarbamide, *thiosinamine*, $NH_2{\cdot}CS{\cdot}NH{\cdot}C_3H_5$, m.p. 74°, is obtained from allyl mustard oil (p. 526) and ammonia. It is readily soluble in water, alcohol and ether. It is converted when heated with mercuric oxide or lead hydroxide into allylcyanamide (sinamine) (p. 529) which polymerizes to triallylmelamine. Hydrogen bromide converts it into the isomeric propylene*pseudo*thiourea (p. 510) (*cf.* Ber. **29**, R. 684).

Diallylthiocarbamide, m.p. 49°, is prepared from allyl mustard oil and allylamine (C. 1898, II. 768).

Reactions of the Alkyl Thioureas.

(1) The thiocarbamides regenerate amines and mustard oils by distillation with P_2O_5, or when heated in HCl-gas :

$$C_2H_5{\cdot}NHCSNHC_2H_5 = C_2H_5N : C : S + NH_2C_2H_5.$$

(2) The sulphur in the alkyl thiocarbamides will be replaced by oxygen if these compounds are boiled with water and mercuric oxide or lead oxide. (*a*) Those that contain two alkyl groups yield the corresponding ureas :

$$(C_2H_5NH)_2CS + HgO = (C_2H_5NH)_2CO + HgS ;$$

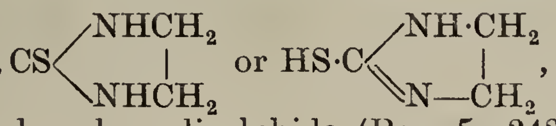
whereas (*b*) the mono-derivatives pass into alkyl cyanamides (and melamines) after parting with hydrogen sulphide (p. 529).

$$C_2H_5NHCSNH_2 = C_2H_5NHC ⋮ N + H_2S.$$

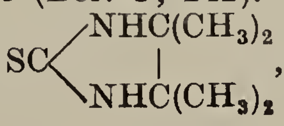
(3) On digesting the dialkyl sulphocarbamides with mercuric oxide and amines, sulphur is exchanged for the imido-group and guanidine derivatives appear (p. 512) :

$$(C_2H_5NH)_2CS + NH_2C_2H_5 + HgO = (C_2H_5NH)_2C : NC_2H_5 + HgS + H_2O.$$

Consult Ber. **23**, 271, upon the constitution of the dialkyl sulphocarbamides.



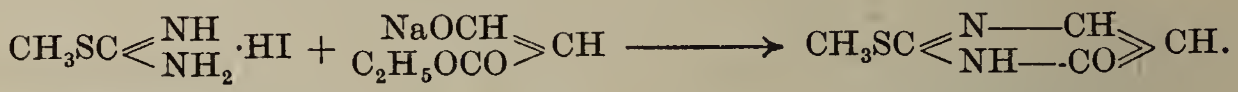
Ethylenethiocarbamide, $CS\left<\begin{array}{l}NHCH_2\\ \quad|\\ NHCH_2\end{array}\right.$ or $HS{\cdot}C\left<\begin{array}{l}NH{\cdot}CH_2\\ \quad|\\ N{-}CH_2\end{array}\right.$, m.p. 195°, is obtained from ethylenediamine and carbon disulphide (Ber. **5**, 242).



Pinacolyl thiocarbamide, carbothiacetonine, $SC\left<\begin{array}{l}NHC(CH_3)_2\\ \quad|\\ NHC(CH_3)_2\end{array}\right.$, m.p. 240–243°, is formed by the action of ammonia on carbon disulphide and acetone (Ber. **29**, R. 669).

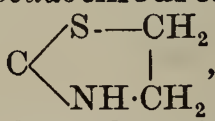
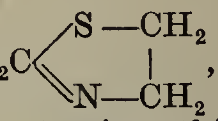
Derivatives of *pseudo*thiocarbamide.—In the preceding derivatives—whether they are derived from the *sym.*- or *unsym.*- sulphocarbamide formula or not—the alkyl groups were in all cases joined to nitrogen, whereas the compounds about to be described must be considered as derivatives of *pseudo*sulphocarbamide.

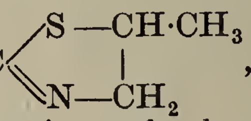
The *alkyl* pseudo*sulphocarbamides* result upon the addition of alkyl iodides to the thioureas. The alkyl groups contained in them are known to be united with sulphur because, when they are acted on with ammonia, they are changed to guanidines and mercaptans. They also easily condense, like the ψ-urea ethers (p. 503), with β-aldo- and β-keto-carboxylic esters into the cyclic derivatives and mercaptopyrimidines, which are hydrolysed into mercaptans and pyrimidines (Ber. **11**, 492: **23**, 2195: C. 1903, I. 1308: 1905, I. 1710):

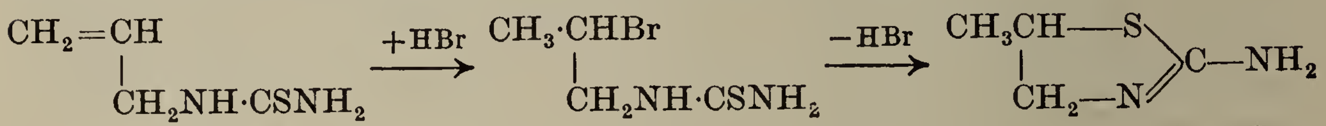


ψ-Methylthiourea hydriodide. Sodium formylacetic ester. Methylthioloxypyrimidine.

Alkylene Derivatives of *pseudo*thiourea.

*Ethylene*pseudo*thiourea*, HN : C, or NH$_2$C, m.p. 85°, is obtained from bromoethylamine hydrobromide and potassium thiocyanate. It is a base with strong basic properties, and its salts crystallize well (Ber. **22**, 1141, 2984: **24**, 260).

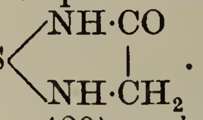
*Propylene*pseudo*thiourea*, NH$_2$C, formed from bromopropylamine and potassium thiocyanate, is perfectly similar. It also results from allylthiourea by action of hydrobromic acid (p. 509):

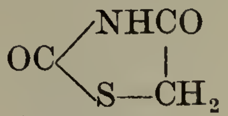


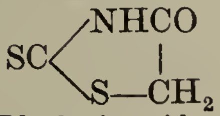
*NNN'S-Tetramethyl*pseudo*thiourea*, MeS·C(: NMe)·NMe$_2$, is a compound containing alkyl groups attached to sulphur and also to both nitrogen atoms. It is a colourless liquid, b.p. 176°, which is obtained from trimethylthiourea and methyl iodide (Bull. Soc. Chim. [4] **7**, 988) or methyl sulphate. This compound and the isomeric tetramethylthiocarbamide (p. 509) yield with methyl iodide the same thiuronium compound (Ann. **438**, 171).

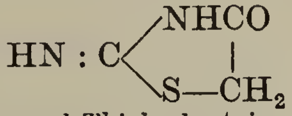
*Acetyl*pseudo*thiourea*, NH$_2$·C(: NH)·S·COCH$_3$, m.p. 165°, is obtained from thiourea by heating it with acetic anhydride; also from cyanamide (carbodiimide, p. 528) and thioacetic acid. This second method argues for the compound being a derivative of *pseudo*sulphocarbamide.

Carbalkoxy carbamides, thio- or *ψ-thio-allophanic esters*, ROOC·NHCSNH$_2$ or ROOC·SC(NH)NH$_2$, is produced by the addition of ammonia or amines to the carbalkoxy thiocarbimides (p. 528) (C. 1901, II. 211), and by the interaction of chlorocarbonic esters on thiourea (C. 1903, I. 1123). *Dithiobiuret*, R$_2$NCS·NR·CSNR$_2$, and *ψ-dithiobiuret*, R$_2$NC(NR)S·CSNR$_2$ (Ber. **37**, 4317).

*pseudo***Thiohydantoin**, C$_3$H$_4$N$_2$S (below), is obtained when chloroacetic acid (Ann. **166**, 383: Ber. **31**, 137) acts on sulphocarbamide, and was formerly thought to be the real thiohydantoin, CS. However, its formation from cyanamide and thioglycollic acid (p. 429) and its decomposition, when boiled with barium hydroxide solution, into thioglycollic acid and dicyandiamide prove that it is a *pseudo*thiocarbamide derivative, which contains the ring occurring in thiazole compounds (Ber. **12**, 1385, 1588). Similar thiazole derivatives result when monochloroacetic acid is replaced by α-bromopropionic acid, bromomaleic acid, and other halogen-carboxylic acids; also when unsaturated acids are employed, such as citraconic acid, to react with thiourea (C. 1897, I. 853). *pseudo*Thiohydantoin crystallizes in long needles, which decompose at about 200°. When boiled with acids, it loses ammonia and is changed into *iso*thiocyanoacetic acid (p. 526). It is closely related to rhodanic acid (p. 507):


*iso*Thiocyano-acetic acid.


Rhodanic acid.

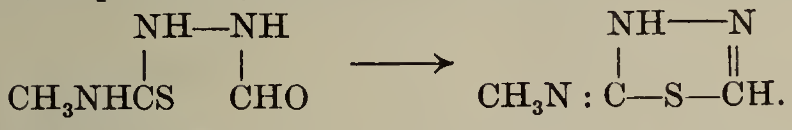

*pseudo*Thiohydantoin.

Alkyl hydroxythioureas are formed by the action of an ethereal solution of anhydrous hydroxylamine and β-alkylhydroxylamines on mustard oil in ether. The monoalkylhydroxythioureas readily decompose into sulphur and alkyl ureas (*cf.* on the contrary phenyl hydroxythiourea (Vol. II)); the dialkyl hydroxythioureas are stable. *Ethylhydroxythiourea*, $C_2H_5NH\cdot CSNOH$, m.p. 109°; sym.-*diethylhydroxythiourea*, $C_2H_5NH\cdot CS\cdot NC_2H_5)OH$, m.p. 81° (Ann. **298**, 117).

Hydrazine Derivatives of Thiocarbonic Acid.—*Dithiocarbazinic acid hydrazine salt*, $NH_2NH\cdot CS\cdot SNH_3\cdot NH_2$, m.p. 124°, is formed by the interaction of hydrazine hydrate and CS_2 (Ber. **29**, R. 233). *α-Carbamyl-β-thiocarbamylhydrazine*, $H_2N\cdot CSNH\cdot NHCONH_2$, m.p. 218–220° (decomp.), is formed from thiosemicarbazide hydrochloride and potassium cyanate (Ber. **29**, 2508). Boiling concentrated hydrochloric acid converts it into *thiourazole*, $\begin{matrix}NHCS\\ NHCO\end{matrix}\!\!>\!NH$, m.p. 177°. *αβ-Dithiocarbamylhydrazine*, $NH_2CSNH\cdot NHCSNH_2$, m.p. 214°, results when a solution of hydrazine sulphate and ammonia thiocyanate is boiled (Ber. **26**, 2877).

Thiosemicarbazide, $\overset{1}{N}H_2\cdot\overset{2}{N}H\overset{3}{C}S\overset{4}{N}H_2$, m.p. 181°, is formed together with αβ-dithiocarbamyl hydrazine (see above), when hydrazine sulphate and ammonium thiocyanate are boiled together in solution. Like semicarbazide (p. 503) it readily reacts with aldehydes and ketones to form *thiosemicarbazones*, $RCH:NNHCSNH_2$, $R_2C:NHNCSNH_2$. They are particularly suitable for isolating aldehydes and ketones on account of the insoluble precipitates given with silver, mercury, and copper salts (Ber. **35**, 2049). 4-*Methylthiosemicarbazide*, $CH_3NH\cdot CSNHNH_2$, m.p. 137°; 2 : 4-*dimethylthiosemicarbazide*, $CH_3NH\cdot CSN(CH_3)NH_2$, m.p. 138°, and 2 : 4-*methylallylthiosemicarbazide*, m.p. 57°, are prepared from hydrazine and methyl hydrazine with methyl and allyl mustard oil respectively. They combine readily with aldehydes (Ber. **37**, 2320). *αβ-Dithiocarbamyl diallylamine*, $C_3H_5NH\cdot CSNH\cdot NH\cdot CSNHC_3H_5$ (Ber. **29**, 859).

Formylmethylthiosemicarbazide, m.p. 167°, yields, with acetyl chloride *methylimidothiobiazoline*, m.p. 245° (Ber. **27**, 622):



Dithiourazole, $\begin{matrix}NH—CS\\ |\quad\quad\\ NH—CS\end{matrix}\!\!>\!NH$, m.p. about 245° (decomp.), is formed on heating αβ-dithiocarbamylhydrazine with hydrochloric acid. The hydrochloride of imidothiourazole, $\begin{matrix}NH\cdot CS—\\ |\quad\quad\quad\\ NH\cdot C(NH)\end{matrix}\!\!>\!NH$, is produced at the same time (Ber. **28**, 949).

Appendix. Potassium diazomethanedisulphonate, $N_2C(SO_3K)_2$, orange-yellow needles, is prepared from *potassium aminomethanedisulphonate*, $NH_2CH(SO_3K)_2$, the addition product of potassium cyanide and two molecules of potassium bisulphite, by means of nitrous acid. With iodine it yields *potassium di-iodomethanedisulphonate*, $I_2C(SO_3K)_2$; and is converted by heat into *potassium azinomethanedisulphonate*, $(SO_3K)_2C:N\cdot N:C(SO_3K)_2$, in the form of colourless crystals. The action of diazobenzene (Vol. II) on the potassium bisulphite compound with potassium diazomethane disulphonate produces *potassium methanedisulphonate phenylhydrazone*, $C_6H_5\cdot NHN:C(SO_3K)_2$ and ultimately *formazylsulphonic acid*, $\begin{matrix}C_6H_5N:N\\ C_6H_5NHN\end{matrix}\!\!\geqslant\!CSO_3H$ (Ber. **29**, 2161).

Guanidine and its Derivatives

Guanidine is, upon the one hand, very closely related to orthocarbonic ester (I) urea and thiocarbamide, and, upon the other, to cyanamide (II) (p. 528), and all are inter-connected by a series of reactions.

$$\text{I.}\ \underset{\text{Ethyl orthocarbonate.}}{C(OC_2H_5)_4} + 4NH_3 \longrightarrow \underset{\text{Unknown.}}{C(NH_2)_4} \longrightarrow \underset{\text{Guanidine.}}{NH : C(NH_2)_2} + NH_3$$

$$\text{II.}\ \underset{\text{Cyanamide.}}{NH_2{\cdot}C \vdots N} + NH_3 \longrightarrow NH : C(NH_2)_2.$$

Guanidine may be regarded as the amidine of carbamic acid, just as the *pseudo*-forms of urea and thiourea, $HO{\cdot}C(: NH){\cdot}NH_2$ and $HS{\cdot}C(: NH){\cdot}NH_2$, are the amidines of carbonic and thiocarbonic acids.

Guanidine, $HN : C(NH_2)_2$, was first obtained (*A. Strecker*, 1861) by the oxidation of guanine (a substance closely related to uric acid, and found in guano) with hydrochloric acid and potassium chlorate. It is found in vetch seeds and in beet-juice (Ber. **29**, 2651). It is also important as the substance from which creatine is derived. It is formed synthetically (1) by heating cyanogen iodide and NH_3, and from cyanamide (p. 528) and ammonium chloride in alcoholic solution at 100° :

$$NH_2{\cdot}C{\equiv}N + NH_4Cl = (H_2N)_2C : NH,HCl.$$

This is analogous to the formation of formamidine from hydrocyanic acid.

(2) It is also produced by heating chloropicrin or (3) esters of orthocarbonic acid, with aqueous ammonia :

$$CCl_3(NO_2) + 3NH_3 = (H_2N)_2C : NH + 3HCl + HNO_2$$
$$C(OC_2H_5)_4 + 3NH_3 = (H_2N)_2C : NH + 4C_2H_5OH.$$

(4) It is most readily prepared from the thiocyanate, which is made by prolonged heating of ammonium thiocyanate to 180–190°, and the further transposition of the thiourea that first forms (Ber. **7**, 92) :

$$2NH_4SNC = 2(H_2N)_2CS = (H_2N)_2C : NH,CNSH + H_2S.$$

The crystals of guanidine are very soluble in water and alcohol, and deliquesce on exposure. Barium hydroxide solution changes it to urea. Guanidine salts of the fatty acids are converted by heat into guanamines, which will be described with the cyanuric compounds (p. 520).

Salts.—Guanidine is a strong base which absorbs carbon dioxide from the air and forms crystalline salts with one equivalent of acid. In these the acid hydrogen becomes attached to the imino-nitrogen thus : $(NH_2)_2C : NHHCl$ (Ann. **438**, 154).

The *nitrate*, $B{\cdot}HNO_3$, forms large plates, sparingly soluble in water. The *hydrochloride*, $B{\cdot}HCl$, forms a *platinichloride* crystallizing in yellow needles. The *carbonate*, $B_2{\cdot}H_2CO_3$, forms quadratic prisms : it reacts alkaline, and has been used for the standardizing of standard acid solutions. The *thiocyanate*, $B{\cdot}HSCN$, crystallizes in large plates, m.p. 118°.

Silver guanidine, $CN_3Ag_2H_3$, H_2O (Ann. **302**, 33).

Alkylguanidines.—Alkylguanidines are formed (1) by heating cyanamide with primary amine hydrochlorides, *e.g.* methylamine hydrochloride yields methylguanidine.

(2) By boiling *sym.*-dialkylthioureas (p. 509) with mercuric oxide and ethylamine in alcoholic solution (Ber. **2**, 601), *e.g.* triethylguanidine.

Ethylguanidine. Picrate, m.p. 180° (Z. physiol. Chem. **154**, 293).

NN′-*Dimethyl*-N′-*ethylguanidine. Picrate*, m.p. 148–152°, (Z. physiol. Chem. **154**, 293).

The alkylguanidines are reconverted into thioureas by heating with carbon bisulphide, the : NH group being replaced by S.

Pentaalkylguanidines are obtained from tetraalkyl*pseudo*thioureas and dialkylamines, preferably in presence of mercuric chloride (Ber. **56**, 1326) :

$$\overset{R_2N}{\underset{RN}{}}\!\geqslant C—SR + HNR_2 \longrightarrow \overset{R_2N}{\underset{RN}{}}\!\geqslant C—NR_2 + RSH.$$

Pentamethylguanidine, m.p. 160°, adds on one mol. of methyl iodide readily, to form hexamethylguanidonium iodide.

Ethyleneguanidine, from cyanogen bromide and ethylenediamine. *Hydrobromide*, m.p. 125° (Ann. Chim. [9] **11**, 361). *Ethylenediguanidine*, from ethylenediamine and *S*-methyl*pseudo*thiourea (Z. physiol. Chem. **155**, 306).

Agmatine, *δ-aminobutylguanidine*, $NH_2{\cdot}C(:NH){\cdot}NH{\cdot}[CH_2]_4{\cdot}NH_2$, the base corresponding to the amino-acid arginine, has a weak insulin-like action on the blood sugar (Naturw. **1927**, 213). Systematic synthetic studies in an attempt to improve this blood-sugar lowering effect of agmatine led to the discovery of *synthalin, decamethylenediguanidine*, $NH_2{\cdot}C(:NH){\cdot}NH{\cdot}[CH_2]_{10}{\cdot}NH{\cdot}C(:NH){\cdot}NH_2$, which has a definite blood-sugar lowering effect (Frank, Nothmann and Wagner, Klin. Wochenschrift, **1926**, 2100). Subsequent investigations have shown that a large part of its action is due to toxic effects on the liver, and it has not fulfilled the original hopes as an insulin substitute effective when taken by mouth.

Vitiatine, *N-methylethylenediguanidine*, $NH_2{\cdot}C(: NH){\cdot}NH{\cdot}[CH_2]_2{\cdot}NMe{\cdot}C(: NH){\cdot}NH_2$, is a base isolated by Kutscher from urine and meat extracts. *Gold salt*, m.p. 167°. Synthesis from cyanamide and *N*-methylethylenediamine, Z. physiol. Chem. **153**, 67 : Z. angew. Chem. **39**, 677).

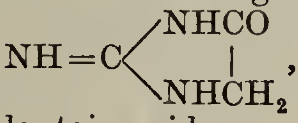
Acylguanidines are obtained by heating guanidine hydrochloride with acid chlorides under pressure (C. 1903, II. 988).

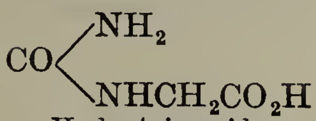
Guanidino Acids.—The important compounds creatine and creatinine belong to this class of substances.

Glycocyamine, guanidinoacetic acid, $NH_2{\cdot}C(: NH){\cdot}NH{\cdot}CH_2{\cdot}COOH$, is obtained by the direct union of glycocoll with cyanamide ; or by heating guanidine carbonate with glycocoll (C. 1905, I. 156) :

$$NH_2(NH)CNH_2 + NH_2CH_2COOH = NH_2(NH)CNHCH_2COOH + NH_3.$$

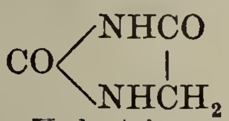
It dissolves with difficulty in cold water and rather readily in hot water, whilst it is insoluble in alcohol and ether. It forms salts with acids and bases. When heated it becomes carbonized without melting.

Glycocyamidine, glycolyl guanidine,  $NH{=}C\begin{cases}NHCO\\ \ \ |\\ NHCH_2\end{cases}$, bears the same relation to glycocyamine as hydantoin to hydantoic acid :



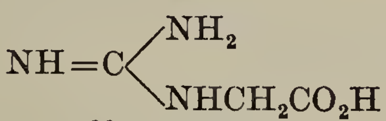
$CO\begin{cases}NH_2\\ NHCH_2CO_2H\end{cases}$

Hydantoic acid.



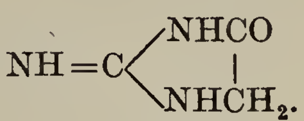
$CO\begin{cases}NHCO\\ \ \ |\\ NHCH_2\end{cases}$

Hydantoin.



$NH{=}C\begin{cases}NH_2\\ NHCH_2CO_2H\end{cases}$

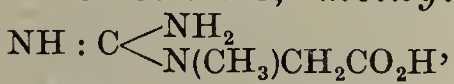
Glycocyamine.



$NH{=}C\begin{cases}NHCO\\ \ \ |\\ NHCH_2.\end{cases}$

Glycocyamidine.

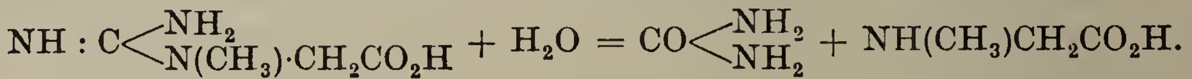
It is produced when glycocyamine hydrochloride is heated to 160° or by the interaction of guanidine and ethyl aminoacetate at 0° (Z. physiol. Chem. **173**, 51).

Creatine, *methylglycocyamine, methylguanidinoacetic acid*,  $NH : C\begin{cases}NH_2\\ N(CH_3)CH_2CO_2H\end{cases}$, was first discovered in 1834 by *Chevreul* in meat extract (κρέας, flesh). *Liebig* (1847) gave it a thorough investigation in his classic research entitled " Ueber die Bestandtheile der Flüssigkeiten des Fleisches " (Ann. **62**, 257). It is found especially in the fluids of muscles and can be prepared from meat extract (Z. physiol. Chem. **112**, 53). It may be prepared artificially (*J. Volhard*, 1869), like glycocyamine, by the union of sarcosine (methyl glycocoll) with cyanamide :

$$CN{\cdot}NH_2 + NH(CH_3){\cdot}CH_2CO_2H = H_2N(NH)C{\cdot}N(CH_3){\cdot}CH_2COOH.$$

Creatine crystallizes with one molecule of water in glistening prisms. Heated to 100°, it loses the water of crystallization. It reacts neutral, and has a faintly bitter taste. It dissolves rather readily in boiling water, but with difficulty in alcohol; and yields crystalline salts with one equivalent of acid.

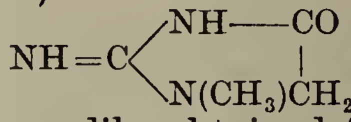
(1) When digested with acids, creatine loses water and becomes changed into creatinine (see below), and (2) with barium hydroxide solution it is converted into urea and sarcosine:



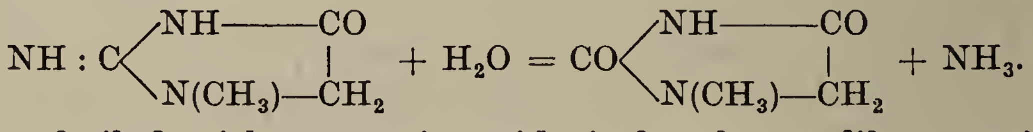
$$NH : C{<}\begin{matrix}NH_2\\ N(CH_3)\cdot CH_2CO_2H\end{matrix} + H_2O = CO{<}\begin{matrix}NH_2\\ NH_2\end{matrix} + NH(CH_3)CH_2CO_2H.$$

Ammonia is liberated at the same time, and β-methylhydantoin is formed. (3) When its aqueous solution is heated with mercuric oxide, creatine yields oxalic acid and methyl guanidine. (4) With acetic anhydride it yields *diacetylcreatine*, m.p. 165° (Ann. **284,** 51).

A derivative of creatine, **phosphocreatine** (*phosphagen*), to which the structure $(HO)_2PO\cdot NH\cdot C(:NH)\cdot NMe\cdot CH_2\cdot COOH$ has been assigned, is of importance in the chemical reactions which take place during muscular contraction (Biochem. J. **21,** 190: J. physiol. **63,** 155: Science, **65,** 401: **67,** 169: J. Biol. Chem. **81,** 629: Naturwissenschaften, **16,** 47: Biochem. Z. **195,** 22).

Creatinine, *methylglycocyamidine,*  $NH=C{<}\begin{matrix}NH—CO\\ \vert\\ N(CH_3)CH_2\end{matrix}$, occurs constantly in urine (about 0·25%, and is readily obtained from creatine by evaporating its aqueous solution, especially when acids are present. It crystallizes in rhombic prisms, and is much more soluble than creatine, in water and alcohol. It is a strong base, which can expel ammonia from ammonium salts and yields well-crystallized salts with acids. It also forms a number of compounds with neutral salts and its *zinc chloride* compound, $(C_4H_7N_3O)_2,ZnCl_2$, is characteristic. The latter is a sparingly soluble crystalline powder precipitated from creatinine solutions by the addition of zinc chloride, and creatinine can be obtained from urine by making use of this compound.

(1) Bases cause creatinine to absorb water and revert to creatine. (2) Boiled with barium hydroxide solution it decomposes into β-methyl hydantoin and ammonia:

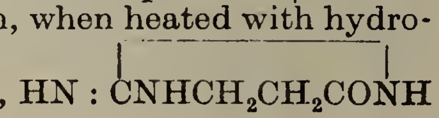


$$NH : C{<}\begin{matrix}NH——CO\\ \vert\\ N(CH_3)—CH_2\end{matrix} + H_2O = CO{<}\begin{matrix}NH——CO\\ \vert\\ N(CH_3)—CH_2\end{matrix} + NH_3.$$

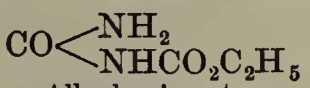
(3) When boiled with mercuric oxide it breaks up like creatine into methyl guanidine and oxalic acid.

When creatinine is heated with alcoholic ethyl iodide, the *ammonium iodide of ethylcreatinine*, $C_4H_7(C_2H_5)N_3O\cdot I$, is produced. Silver oxide converts this into the ammonium base, $C_4H_7(C_2H_5),N_3O\cdot OH$.

Creatinol, $NH_2\cdot C(:NH)\cdot NMe\cdot CH_2\cdot CH_2OH$, is obtained from *pseudo*thiourea ethers and methylaminoethanol (Z. angew. Chem. **39,** 677).

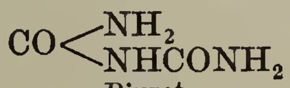
α-Guanidinopropionic acid, $(N_2H_3)C\cdot NH\cdot CH(CH_3)COOH$, m.p. 180°. *β-Guanidinopropionic acid,* m.p. 206–213°, with decomposition, when heated with hydrochloric acid yields the hydrochloride of *β-alacreatinine*,  $HN : \overline{C NHCH_2CH_2CONH}$ (C. 1905, I. 156).

Guaneides of Carbonic Acid.—Guanoline, guanyl urea, biguanide, and probably dicyandiamide, corresponding with allophanic ester, biuret, and cyanurea (p. 502), are derivatives of the guaneide of carbonic acid. This is not known, and probably cannot exist :



$\mathrm{CO}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NHCO_2C_2H_5}\end{matrix}$

Allophanic ester.

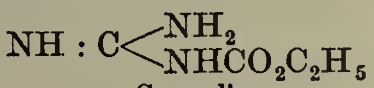


$\mathrm{CO}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NHCONH_2}\end{matrix}$

Biuret.

$\mathrm{CO}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NHCN}\end{matrix}$

Cyanurea.

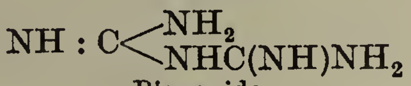


$\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NHCO_2C_2H_5}\end{matrix}$

Guanoline.

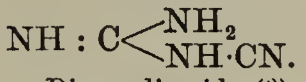
$\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NHCONH_2}\end{matrix}$

Guanyl urea.



$\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NHC(NH)NH_2}\end{matrix}$

Biguanide.



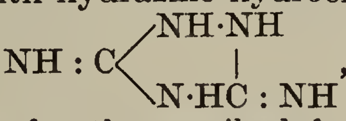
$\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH{\cdot}CN.}\end{matrix}$

Dicyandiamide (?).

Guanoline, *guanidinocarboxylic ester*, $\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NHCO_2C_2H_5}\end{matrix} + \frac{1}{2}H_2O$, m.p., dehydrated, 114°. It is obtained from guanidodicarbonic diethyl ester, $NH : C(NH{\cdot}CO_2C_2H_5)_2$, m.p. 162°, the reaction-product arising from chlorocarbonic ester and guanidine, through the action of ammonia (Ber. **7**, 1588).

Dicyandiamidine, *guanylurea*, $\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH{\cdot}CO{\cdot}NH_2}\end{matrix}$, is formed (1) by the action of dilute acids on dicyandiamide or cyanimide, or (2) by fusing a guanidine salt with urea (Ber. **7**, 446), (3) from urea by heating it with benzene sulphochloride, whereby it is obtained as a benzene sulphonate (C. 1901, I. 885). It is a strongly basic, crystalline substance. It forms a *copper* derivative having a characteristic red colour, and a yellow *nickel* compound, $M(N_4H_5OC_2)_2 + H_2O$ (Ber. **39**, 3356). When digested with barium hydroxide solution it decomposes into CO_2, $2NH_3$, and urea (Ber. **20**, 68).

Biguanide, *guanylguanidine*, $\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NHC(NH)NH_2}\end{matrix}$, is formed (1) on heating guanidine hydrochloride to 180–185° ; (2) when cyanoguanidine is heated with ammonium chloride. It is a strongly alkaline base, forming a *copper* derivative with characteristic red colour. Chloroform and alkali hydroxide convert it into formoguanamine (p. 531).

Dicyandiamide, *param*, *cyanoguanidine*, $\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH{\cdot}CN}\end{matrix}$, m.p. 205°, results from the polymerization of cyanamide upon long standing or by evaporation of its aqueous solution, and can easily be prepared from technical calcium or sodium cyanamide (p. 529) (C. 1905, II. 1530, etc.). Contrary to the two substances described above, it is a neutral body. Ammonia converts it into biguanide ; dilute acids into guanyl urea. With piperidine it forms a biguanide derivative (Ber. **24**, 899 : **25**, 525), with hydrazine hydrochloride when heated in alcoholic solution it gives *guanazole*,  $\mathrm{NH : C}\Big\langle\begin{matrix}\mathrm{NH{\cdot}NH}\\ |\\ \mathrm{N{\cdot}HC : NH}\end{matrix}$, m.p. 206° (Ber. **27**, R. 583) ; both reactions form a basis for the ascribed formula.

Thiocyanodiamidine, *guanylthiourea*, $NH_2CSNHC(NH)NH_2$, is obtained from thiourea and PCl_5 or thiophosgene. It is isomerized at 100° to guanidine thiocyanate. Silver salts produce dicyanodiamide with loss of H_2S (*cf.* Ber. **36**, 3322).

Nitro-, amino-, and Hydroxy-guanidines and their transposition products.

Of these substances, nitroguanidine is the most suitable material for the preparation of a series of remarkable guanidine and urea derivatives (*Thiele*, Ann. **270**, 1 : **273**, 133 : Ber. **26**, 2598, 2645).

Nitroguanidine, $NH_2{\cdot}C(:NH){\cdot}NHNO_2$, m.p. 230°, results on treating guanidine with a mixture of nitric and sulphuric acids. It dissolves with difficulty in cold water, more readily in hot water, and particularly freely in alkalis, because of its feeble acid character.

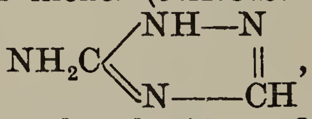
Nitrosoguanidine, $NH_2{\cdot}C(:NH){\cdot}NH{\cdot}NO$ (?), is produced by reducing nitroguanidine with zinc dust and sulphuric acid. It consists of yellow needles, which explode at 160–165°.

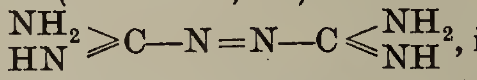
Aminoguanidine, $NH_2{\cdot}C(:NH){\cdot}NH{\cdot}NH_2$, results when nitro- and nitrosoguanidine are reduced with zinc dust and acetic acid, or by electrolysis in neutral solution with a zinc cathode (C. 1906, I. 1066), and can be precipitated as a slightly soluble bicarbonate (Ann. **302**, 333). Free aminoguanidine decomposes readily when boiled with acids, with the intermediate formation of semicarbazide (p. 503), into carbonic acid, ammonia, and hydrazine, which can therefore be conveniently prepared in this manner :

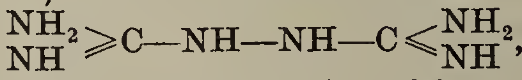
$$\mathrm{NH:C}{<}\begin{matrix}\mathrm{NHNH_2}\\ \mathrm{NH_2}\end{matrix} \xrightarrow{\mathrm{H_2O}} \mathrm{CO}{<}\begin{matrix}\mathrm{NHNH_2}\\ \mathrm{NH_2}\end{matrix} \xrightarrow{\mathrm{H_2O}} \mathrm{CO_2} + \begin{matrix}\mathrm{NH_2NH_2}\\ \mathrm{NH_3}\end{matrix}$$

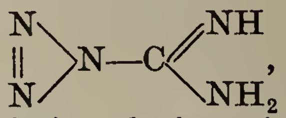
Aminoguanidine forms well-crystallized compounds with dextrose, galactose, and lactose and many other aldehydes and ketones (Ber. **28**, 2613). Glyoxal and α-diketones with aminoguanidine lose water and form bis-aminoguanidones (Ann. **302**, 275) : aromatic diketones, on the other hand, yield 1 : 2 : 4-triazine derivatives (Ann. **302**, 275, 301 : J. Indian Chem. Soc. **4**, 183).

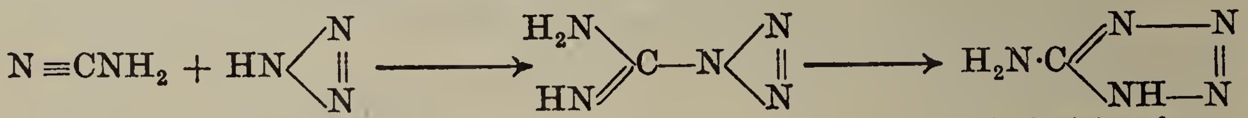
Nitroaminoguanidine, $\mathrm{NO_2{\cdot}NH{\cdot}C(:NH){\cdot}NH{\cdot}NH_2}$, is obtained from nitroguanidine and hydrazine in dilute aqueous solution at 50–60°. It decomposes explosively at its melting point and forms explosive copper and silver derivatives. Its *nickel salt* in alkaline solution has a blue colour, and its formation provides a delicate test for nickel (J.A.C.S. **50**, 2465).

Aminotriazole,  , m.p. 159°, is formed from formyl aminoguanidine nitrate and soda (Ann. **303**, 33). See also Guanazole (above).

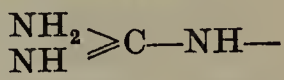
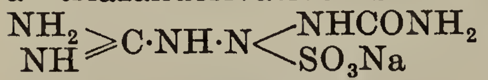
Azodicarbondiamidine,  $\begin{matrix}\mathrm{NH_2}\\ \mathrm{HN}\end{matrix}{\geqslant}\mathrm{C{-}N{=}N{-}C}{\leqslant}\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH}\end{matrix}$, is obtained as *nitrate* when aminoguanidine nitrate is oxidized with $\mathrm{KMnO_4}$. The nitrate forms a yellow, sparingly soluble, crystalline powder, which explodes at 180–184°. It passes into azodicarbonamide (p. 504) when boiled with water.

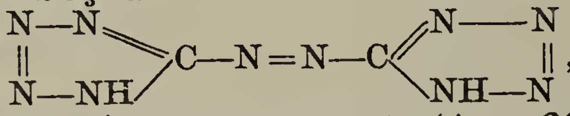
Hydrazodicarbonamidine,  $\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH}\end{matrix}{\geqslant}\mathrm{C{-}NH{-}NH{-}C}{\leqslant}\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH}\end{matrix}$, results as nitrate when azodicarbonamidine nitrate is reduced with $\mathrm{H_2S}$.

Azidocarbamidine, carbamide imidazide,  , corresponds with carbamic acid azide (p. 504). It is only stable in solution, since it very readily isomerizes into aminotetrazole (see below) : *nitrate*, $\mathrm{(CN_5H_3)HNO_3}$, m.p. 129°, is obtained from aminoguanidine and potassium nitrite in nitric acid solution, in the form of colourless crystals. Excess of sodium hydroxide solution converts it partially into cyanamide and hydrazoic acid. These substances unite in aqueous solution probably to re-form azidocarbamidine, which is simultaneously isomerized to aminotetrazole (Ann. **314**, 339) :

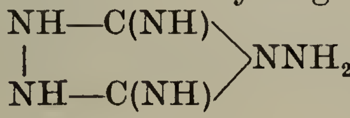


Cyanamide. Hydrazoic acid. Aminotetrazole.

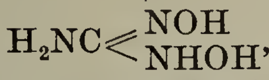
Diazoguanidine cyanide, amino-imino-methyl cyanotriazene,  $\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH}\end{matrix}{\geqslant}\mathrm{C{-}NH{-}}$ $\mathrm{N{=}N{\cdot}CN}$, is produced from azidocarbamidine nitrate and potassium cyanide. The amide, obtained from the nitrile, takes up bisulphite and forms a triazanderivative—sodium triazandicarboxylic amidine amidosulphonate,  $\begin{matrix}\mathrm{NH_2}\\ \mathrm{NH}\end{matrix}{\geqslant}\mathrm{C{\cdot}NH{\cdot}N}{<}\begin{matrix}\mathrm{NHCONH_2}\\ \mathrm{SO_3Na}\end{matrix}$ (Ann. **305**, 64, 80).

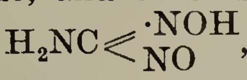
Azotetrazole,  , results when aminotetrazole is oxidized by potassium permanganate (Ann. **303**, 57).

iso*Cyanotetrabromide* or *tetrabromoformalazine*, $\mathrm{Br_2C{=}N{-}N{=}CBr_2}$, m.p. 42°, is produced when hydrazotetrazole, the reduction-product of azotetrazole, is treated with bromine (Ber. **26**, 2645). With alkalis *iso*cyanotetrabromide apparently yields iso*cyanoxide*, $\mathrm{CO{=}N{-}N{=}CO}$ (?), or a polymer of it. Should an oxidizable body like alcohol be present, *iso*cyanogen, $\mathrm{C{=}N{-}N{=}C}$ (?), is produced. This substance has an odour very much like that of *iso*nitriles. Sodium ethoxide converts *iso*cyanotetrabromide into *azimethyl carbonate* $\mathrm{(CH_3O)_2C{=}N{-}N{=}C(OCH_3)_2}$ (Ann. **303**, 71).

Diaminoguanidine, $HN : C(NHNH_2)_2$, obtained as a hydrochloride or hydrobromide by the action of cyanogen chloride or bromide on hydrazine. *Dibenzaldiaminoguanidine*, $HN : C(NHN : CHC_6H_5)_2$, m.p. 180°, exists as yellow needles. Hydrazine and two molecules of cyanogen bromide form *guanazine*, $HN : C(NHNH)_2C : NH$, or  $\left.\begin{matrix} NH{-}C(NH) \\ | \\ NH{-}C(NH) \end{matrix}\right\rangle NNH_2$ (Ber. **37**, 4524 : C. 1905, II. 122).

Triaminoguanidine, $H_2N{\cdot}N : C(NHNH_2)_2$; its hydrochloride is obtained by heating hydrazine hydrate with carbon tetrachloride in a stream of ammonia. *Tribenzal triaminoguanidine*, $C_6H_5CH : NN : C(NHN : CHC_6H_5)_2$, m.p. 196°, is hydrolysed into benzaldehyde, hydrazine, and carbohydrazide (p. 504) (Ber. **37**, 3548).

Dihydroxyguanidine,  $H_2NC{<}\begin{matrix} NOH \\ NHOH \end{matrix}$, is obtained as hydrobromide from cyanogen bromide and hydroxylamine in methyl alcohol. It is stable to acids, but is changed immediately by alkalis into an unstable red *azo body*, which becomes ultimately converted into azoxybismethenylamidoxime, $H_2NC(NOH){\cdot}(N_2O)C(NOH)NH_2$, hydrazodicarbonamide, and other substances.

Amino-methyl-nitrosilic acid,  $H_2NC{<}\begin{matrix} {\cdot}NOH \\ NO \end{matrix}$, is produced when alcoholic potassium hydroxide decomposes the above-mentioned intermediate azo-body. It consists of very unstable green tabular crystals, and combines to form blue or green salts ; *potassium salt* is deposited from alcohol as steel-blue brilliant needles (Ber. **38**, 1445).

Nitriles and Imides of Carbonic and Thiocarbonic Acids

The compounds cyanic acid, thiocyanic acid, cyanogen chloride and cyanamide can be represented as the nitriles of carbonic, thiocarbonic, chloroformic and carbamic acids.

$HO{\cdot}COOH$	$HS{\cdot}COOH$	$Cl{\cdot}COOH$	$NH_2{\cdot}COOH$
Carbonic acid.	Thiocarbonic acid.	Chloroformic acid.	Carbamic acid.
$HO{\cdot}CN$	$HS{\cdot}CN$	$Cl{\cdot}CN$	$NH_2{\cdot}CN$
Cyanic acid.	Thiocyanic acid.	Cyanogen chloride.	Cyanamide.

For the nitriles, with the exception of cyanogen chloride, another formulation is possible :

$HN : CO$	$HN : CS$	$HN : C : NH$
*iso*Cyanic acid.	*iso*Thiocyanic acid.	Carbodiimide.

Alkyl derivatives are known corresponding to both formulæ of each of these compounds, and their constitution is made clear by their reactions, but for the free acids and free cyanamide the problem is not so simple. To thiocyanic acid the normal formula $N \vdots C{\cdot}SH$ is usually ascribed, but to cyanic acid itself the *iso*-formula $HN : C : O$ on the grounds of the formation of *iso*cyanic esters by the action of diazomethane (C. 1906, II. 1723).

Cyanamide and cyanic acid possess a remarkable tendency to polymerization, the former yielding dicyandiamide and tricyantriamide (melamine), the latter cyamelide and cyanuric acid. The polymers will be discussed after the corresponding monomeric compound.

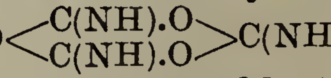
Oxygen Derivatives of Cyanogen, their Isomerides and Polymerides

Cyanic acid, $HN : CO$ or $HO{\cdot}C \vdots N$, isomeric with fulminic acid or carbyloxime (p. 294), is obtained by heating the polymeric cyanuric acid. The vapours which distil over are condensed in a strongly cooled receiver.

The acid is only stable below 0°, and is a mobile, very volatile liquid, which reacts strongly acid, and smells very much like glacial acetic acid. It produces blisters upon the skin. At about 0°, the aqueous solution is rapidly converted into carbon dioxide and ammonia:

$$HONC + H_2O = CO_2 + HN_3.$$

At 0°, the liquid cyanic acid passes rapidly into the polymeric *cyamelide*—a white, porcelain-like mass, which is insoluble in water, and when distilled reverts to cyanic acid. Above 0°, the conversion of liquid cyanic acid into cyamelide and cyanuric acid (C. 1902, I. 526) occurs, accompanied by an explosive generation of vapour (*cf.* Formaldehyde, p. 233). Cyanic acid dissolves in alcohols, yielding esters of allophanic acid (p. 501).

Cyamelide is also obtained by grinding together potassium cyanate and crystallized oxalic acid, and washing out with water. It is a loose white powder, only slightly soluble in all solvents. Prolonged boiling with water decomposes it into NH_3, CO_2, and partly into cyanuric acid (p. 520). When digested with concentrated sodium hydroxide solution it is converted completely into tri-sodium cyanurate. This probably corresponds with the formula  $O{<}\begin{matrix}C(NH).O\\C(NH).O\end{matrix}{>}C(NH)$; it is therefore analogous to trioxymethylene (p. 236) (Ber. **38**, 1013).

Potassium cyanate, *potassium* iso*cyanate*, (*ordinary potassium cyanate*), $KO{\cdot}C⋮N$ or $KN:C:O$, is formed in the oxidation of potassium cyanide in the air, or with some oxidant like lead oxide, minium, potassium permanganate (Ber. **36**, 1806), or sodium hypochlorite (Ber. **26**, R. 779). It is most conveniently made by heating small portions (3–5 gm.) of an intimate mixture of 100 parts potassium ferrocyanide and 75 parts of potassium bichromate in an iron dish, during which NH_3 should not be set free (Ber. **26**, 2438). It results, too, on conducting cyanogen or cyanogen chloride into potassium hydroxide solution (Ber. **23**, 2201). Alkali cyanates have more recently been manufactured by the direct combination of disodium cyanamide with carbon dioxide at high temperatures: $Na{\cdot}N:C:N{\cdot}Na + CO_2 \xrightarrow{\quad} 2Na{\cdot}N:CO$ (Z. angew. Chem. **38**, 642: *cf.* cyanide manufacture, p. 287).

The salt crystallizes in shining leaflets, resembling potassium chlorate, or in quadratic plates (Ber. **27**, 837), and dissolves readily in cold water, but with difficulty in hot alcohol. In aqueous solution it decomposes rapidly into ammonia and potassium carbonate.

Potassium cyanate precipitates aqueous solutions of the heavy metals. The *lead*, *silver*, and *mercurous* salts are white, the *cupric* salt is green in colour. Lead cyanate is quantitatively hydrolysed to carbonate and urea when boiled with water (C. 1904, I. 160).

Ammonium cyanate, $NH_4{\cdot}OC⋮N$ or $NH_4{\cdot}N:C:O$, is a white crystalline powder, formed by contact of cyanic acid vapours with dry ammonia, or by mixing ethereal solutions of cyanic acid and ammonia (C. 1900, I. 107). Potassium hydroxide decomposes it into potassium cyanate and ammonia. On heating the dry salt to 60°, or by evaporating its aqueous solution, it passes into the isomeric urea (p. 494).

The cyanates of the primary and secondary amines are similarly converted into alkylureas, whereas the salts of the tertiary amines remain unchanged.

Esters of normal cyanic acid, *cyanetholines,* RO—C≡N, are not known (Ann. **287,** 310). Imidocarbonic acid esters (p. 501) are produced when cyanogen chloride acts on sodium alcoholates in alcoholic solution.

Esters of isoCyanic Acid, *Alkyl Carbimides* or *Alkyl* iso*Cyanates.*—*Wurtz* prepared these, in 1848, (1) by distilling potassium ethyl sulphate with potassium cyanate:

$$(C_2H_5)KSO_4 + KN:CO = C_2H_5N:CO + K_2SO_4.$$

Better yields are obtained by the use of dimethyl or diethyl sulphate (Ber. **58,** 1320). Cyanuric esters are simultaneously produced in this reaction.

(2) *iso*Cyanic esters are also produced by oxidizing the carbylamines with mercuric oxide:

$$C_2H_5{\cdot}NC + O = C_2H_5{\cdot}N:CO;$$

(3) by the action of silver cyanate on alkyl iodides at low temperatures (together with esters of cyanuric acid, p. 520):

$$C_2H_5I + AgN:CO = C_2H_5N:CO + AgI;$$

and (4) by heating the dry mercuric chloride double salt of the alkyl carbamine thiolic acids (p. 506) (Ann. **359,** 202):

$$C_2H_5NH{\cdot}CO{\cdot}S{\cdot}HgCl \longrightarrow C_2H_5N:CO + HgS + HCl.$$

These esters are volatile liquids, boiling without decomposition, and possessing a very disagreeable, penetrating odour, which provokes tears. They dissolve without decomposition in ether. On standing they pass rather rapidly into the polymeric *iso*cyanuric esters.

iso*Cyanic methyl ester,* $CH_3N:CO$, *methyl* iso*cyanate, methyl carbimide,* b.p. 44°; *ethyl ester,* $C_2H_5N:CO$, b.p. 60°; *allyl ester,* $C_3H_5N{\cdot}CO$, b.p. 82°; iso*butyl ester,* $CONC_4H_9$, b.p. 101°.

Reactions.—In all their reactions they behave like carbimide derivatives, in which the alkyl group is united to nitrogen.

(1) Heated with KOH they yield primary amines and potassium carbonate (p. 190). This is the method Wurtz used when he first discovered the amines.

(2) Acids in aqueous solution behave similarly:

$$C_2H_5N:CO + H_2O + HCl = CO_2 + C_2H_5NH_2{\cdot}HCl.$$

(3) With the amines and ammonia they yield alkylureas (*q.v.*).

(4) Water decomposes them at once into CO_2 and dialkylureas. In this decomposition amines form first, CO_2 being set free, and these combine with the excess of *iso*cyanic ester to dialkylureas (*q.v.*).

(5) Fatty acids convert them into primary acid alkylamides, $R{\cdot}CO{\cdot}NHR'$ (p. 322), CO_2 being simultaneously evolved.

(6) Acid anhydrides convert them into *secondary* acid alkylamides, $(R{\cdot}CO)_2NR'$, (p. 322).

(7) The esters of *iso*cyanic acid unite with alcohols, yielding esters of alkylcarbamic acids (p. 492).

(8) As derivatives of ammonia the *iso*cyanic esters are capable of combining directly with the halogen acids. The products are

alkylcarbamyl chlorides (p. 493), from which the *iso*cyanic esters are again separated by distillation with lime:

$$C_2H_5NCO \underset{Ca(OH)_2}{\overset{HCl}{\rightleftarrows}} C_2H_5\cdot HNCO\cdot Cl.$$

Glycocollic ester isocyanate, $OC:NCH_2CO_2C_2H_5$, b.p. 115–120°/15 mm., is obtained from glycocollic ester hydrochloride by excess of phosgene in toluene. Water converts it into *carbiminodiacetic acid*, $CO(NHCH_2CO_2H)_2$, m.p. 167°. Other amino-acids yield corresponding mixed urea derivatives (C. 1906, II. 671).

Acetyl isocyanate, $OC:N\cdot COCH_3$, b.p. 80°, is prepared by the action of acetyl chloride on mercury fulminate (p. 295), and on silver cyanate (Ber. **36**, 3214). Alcohol and ammonia convert it respectively into acetylurethane (p. 491) and monoacetyl urea (p. 498).

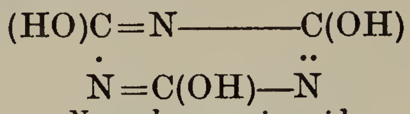
Methanesulphonyl isocyanate, $CH_3SO_2N:CO$, m.p. 31°, b.p. 73·5–75°/10 mm. (Ber. **38**, 2015).

Carbethoxyl isocyanate, $C_2H_5OCO\cdot N:CO$, b.p. 116°, is produced from nitrogen tricarboxylic ester (p. 502) by means of P_2O_5. It unites with alcohol to form imido-dicarboxylic ester (p. 501); and with ammonia to form allophanic ester (p. 501). Water converts it to carbonyl diurethane (p. 502) (Ber. **39**, 686).

Cyanuric Acid and its Alkylic Derivatives

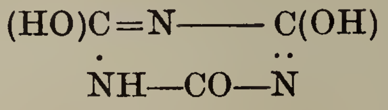
As with cyanic acid, so with tricyanic acid, more than one formula is possible:

(1)

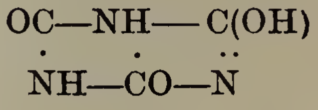


Normal cyanuric acid.

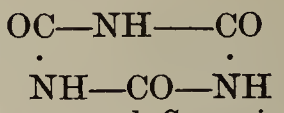
(2)



(3)



(4)



iso- or *pseudo*-Cyanuric acid.

Ordinary solid cyanuric acid, like cyanic acid, is most probably to be represented by the imide, or *iso*cyanuric formula (4). When titrated with sodium hydroxide and phenolphthalein in aqueous solution, it behaves as a monobasic acid, yielding salts according to formula (3). Two equivalents of alkali produce dibasic salts, corresponding with formula (2), which, on boiling, take up a third equivalent of the metal and form stable, well-crystallizing tribasic salts, $C_3N_3O_3M_3$ (formula 1), some of which are only slightly soluble in water. Corresponding with these consecutive desmotropic transformations (p. 49), the temperature coefficient of the electrical conductivity (taken as of a monobasic acid) of an aqueous solution of cyanuric acid increases with increasing temperature: the acid becomes stronger by a change of constitution as from formula 4 to 1 (Ber. **39**, 139). Its behaviour as a *pseudo*-acid is shown by the occurrence of isomeric mercury salts: O-*mercury cyanurate*, $C_3N_3(Ohg)_3$, obtained from trisodium cyanurate and mercury salts, is decomposed by alkalis; N-*mercury cyanurate*, $C_3O_3(Nhg)_3$, is produced from free cyanuric acid and mercury salts, and is not decomposed by alkalis (Ber. **35**, 2717) ($hg = \frac{1}{2}Hg$.)

Esters can be obtained from all four formulæ, but only those in which the alkyl group is united to oxygen can be decomposed by alkalis (Ber. **38**, 1005). The cyanuric halides (p. 523) are derived from formula 1.

Cyanuric acid, $C_3N_3O_3H_3$, was first observed by Scheele in the dry distillation of uric acid. It is produced (1) by heating tricyanogen chloride, $C_3N_3Cl_3$, or bromide (Ber. **16**, 2893) with water to 120–130°, or with alkalis. (2) Dilute acetic acid added to a solution of potassium cyanate gradually separates primary potassium cyanurate, $C_3N_3O_3H_2K$, from which mineral acids liberate cyanuric acid. (3) It is formed, also, (*a*) on heating urea (*b*) or carbonyldiurea (p. 502); (*c*) on conducting chlorine over urea heated to 130–140°; (*d*) when urea is heated with a solution of phosgene in toluene to 190–230° (Ber. **29**, R. 866).

(*a*) $3CO(NH_2)_2 = C_3O_3N_3H_3 + 3NH_3$
(*b*) $NH_2CONH{\cdot}CO{\cdot}NHCONH_2 = C_3O_3N_3H_3 + NH_3$
(*c*) $3Cl + 3CO(NH_2)_2 = C_3O_3N_3H_3 + 2NH_4Cl + HCl + N$
(*d*) $3COCl_2 + 3CO(NH_2)_2 = 2C_3O_3N_3H_3 + 6HCl$.

The evidence in favour of a symmetrical structure for cyanuric acid depends on the successive substitution of the three chlorine atoms of cyanuric chloride by amino-, methylamino-, and ethylamino-groups, which always leads to the same end-product, $C_3H_3(NH_2)(NHCH_3)(NH{\cdot}C_2H_5)$, whatever the order in which the three groups are introduced (Ber. **32**, 692).

Cyanuric acid crystallizes from aqueous solution with 2 molecules of water ($C_3N_3O_3H_3 + 2H_2O$) in large rhombic prisms. It is soluble in 40 parts of cold water, and easily soluble in hot water and alcohol. When boiled with acids it decomposes into carbonic acid and ammonia; when distilled it breaks up into cyanic acid. PCl_5 converts it into tricyanogen chloride.

Characteristic salts of the tribasic cyanuric acid are the trisodium salt and the amethyst-coloured *cuprammonium salt* (see above).

Normal cyanuric esters are formed (1) by the action of cyanogen chloride on sodium alcoholates.

(2) A simpler procedure is to act on the sodium alcoholates with cyanuric chloride or bromide (Ber. **18**, 3263 and **19**, 2063).

Methyl cyanurate, m.p. 135°, b.p. 263°.

Ethyl cyanurate, m.p. 29°, b.p. 275°.

The normal cyanuric esters, on being digested with the alkalis, break up into cyanuric acid and alcohol. They combine with six atoms of bromine. PCl_5 converts them into cyanuric chloride. Boiling gradually changes them to *iso*cyanuric esters.

Partial hydrolysis of the normal cyanuric esters by NaOH or $Ba(OH)_2$ gives rise to normal dialkylcyanuric acids, which, when heated, rearrange themselves into dialkyl *iso*cyanuric acids (Ber. **19**, 2067):

O-*Dimethylcyanuric acid*, $C_3N_3(OCH_3)_2{\cdot}OH$, m.p. 160–180°. O-*Dimethylcyanuric acid chloride*, $C_3N_3(OCH_3)_2Cl$, m.p. 81°, is prepared from cyanuric chloride, methyl alcohol and zinc dust (Ber. **36**, 3195).

Esters of *iso*cyanuric acid, *tricarbimide esters*, $C_3O_3(NR)_3$, are formed together with the *iso*cyanic esters, when the latter are prepared by the distillation of potassium cyanate with salts of alkylsulphuric acid (p. 168). We have already spoken of their formation as a result of the molecular transposition of the cyanuric esters. Hence they are formed together with these, or appear in their stead in energetic reactions—*e.g.* in the distillation of potassium cyanate with ethyl sulphate, or when silver cyanurate is acted upon by alkyl iodides (Ber. **30**, 2616). They are solid crystalline bodies, soluble in water, alcohol, and ether, and may be distilled without decomposition. They pass into primary amines and potassium carbonate when boiled with alkalis, similarly to the *iso*cyanates:

$$C_3O_3(NCH_3)_3 + 6KOH = 3K_2CO_3 + 3NH_2CH_3.$$

Methyl iso*cyanurate, trimethylcarbimide*, $C_3O_3(NCH_3)_3$, m.p. 176°, b.p. 296°.

Ethyl iso*cyanurate*, $C_3O_3(NC_2H_5)_3$, m.p. 95°, b.p. 276°. It volatilizes with steam.

Mixed *normal-iso***Cyanuric Esters.** OON-*Trimethyl cyanurate*, $CH_3N{<}\begin{array}{l}CO\text{———————}N\\C(OCH_3){=}N\end{array}{>}C(OCH_3)$, m.p. 105°, is prepared, together with other bodies, from silver cyanate and iodomethane by prolonged contact in the cold. It can be sublimed undecomposed in the cold, and is hydrolysed by hydrochloric acid into *ψ-methyl cyanuric acid*, $CH_3N(C_3O_3N_2H_2)$, m.p. 296°. This also results from the action of boiling alkalis on carbonyl dimethyl urea (p. 502).

ONN-*Trimethyl cyanurate*, $CH_3N{<}\begin{array}{l}CO{-}N(CH_3)\\CO{-}N{=\!=\!=}\end{array}{>}C(OCH_3)$, m.p. 118°, is produced from silver cyanurate and iodomethane in the cold. Hydrolysis gives rise to *dimethyl-ψ-cyanuric acid*, $(CH_3N)_2(C_2O_3NH)$, m.p. 222°, which is also obtained by heating *n*-dimethyl cyanuric acid (see above) (Ber. **38**, 1005).

Cyanuric triacetate, $C_3N_3O_3(COCH_3)_3$, m.p. 175° with decomposition, is produced from silver cyanurate and acetyl chloride.

Cyanuric tricarbonic ester, $(C_3N_3O_3)(CO_2C_2H_5)$, results from the polymerization of cyanocarbonic acid ester (p. 540). It is very slightly soluble, except in chloroform (Ber. **38**, 1010).

Cyanuric triurea, $(C_3N_3O_3)(CONH_2)_3$, is formed, together with cyanuric acid, when urea is heated to 200°, or with cyanuric bromide. It is amorphous and slightly soluble. It forms a *trisodium* salt, which crystallizes with $5H_2O$ (Ber. **38**, 1010).

Halogen Compounds of Cyanogen and its Polymers

The halogen compounds of cyanogen result from the action of halogens on metallic cyanides, such as mercury cyanide, and on aqueous hydrocyanic acid. The chloride and bromide condense to tricyanides in which the C_3N_3 group $\begin{array}{c}{-}C{=}N{-}C{-}\\|\qquad\quad|\\N{=}C{-}N\end{array}$ constitutes the radical of normal cyanuric acid. On account of their connection on the one hand with cyanic and cyanuric acids and on the other with hydrocyanic acid and its salts, the cyanogen halides can be looked on as being either halogen compounds of the anhydride of *n*-cyanic acid or the halogen imides of carbon monoxide, *e.g.*:

$HN{=}C$	$ClN{=}C$ or $ClC{\equiv}N$	$HOC{\equiv}N$
Hydrocyanic acid. Carbonyl imide.	Cyanogen chloride.	*n*-Cyanic acid.

The formula $XN:C$ receives substantiation from the fact that cyanogen halides easily yield hydrocyanic acid; also that the cyanogen chloride and alcoholic sodium ethoxide do not yield the normal cyanic ester (p. 519), but imidocarbonic ether, a reaction which is best explained as taking place with the intermediate formation of NaNC and an alkyl hypochlorite (p. 169) (C. 1902, I. 525, 862). Contrary to this is the reaction of cyanogen chloride with mercaptides to form alkyl thiocyanates (p. 525), and with ammonia to produce cyanamide (p. 528).

Cyanogen Halides.—*Cyanogen chloride*, CNCl, m.p. −5°, b.p. 15°, is produced by the action of chlorine on aqueous hydrocyanic acid or on a cold mercuric cyanide solution, or better, on a solution of potassium cyanide and zinc sulphate (C. 1907, I. 746). It is a mobile liquid. After some time it passes spontaneously into cyanuric chloride. With ammonia, it yields ammonium chloride and cyanamide, $NH_2{\cdot}NC$. Alkalis decompose it into metallic cyanides and *iso*cyanates.

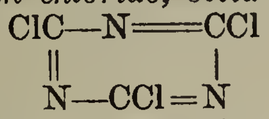
Cyanogen bromide, CNBr, m.p. 52°, b.p. 61°, is produced on adding a potassium cyanide solution drop by drop to bromine, when well cooled (Ber. **29**, 1822). For the reaction of cyanogen bromide and tertiary amines, see p. 196, etc. Cyanogen bromide is used in the preparation of aromatic hydroxy-aldehydes (Helv. Chim. Acta. **2**, 89) and for the preparation of aromatic nitriles, by the use of aluminium chloride (Helv. Chim. Acta. **2**, 482).

Cyanogen iodides, CNI, sublimes at 45°, without melting, in brilliant white needles.

These compounds are sparingly soluble in water, but they dissolve readily in alcohol and ether. Their vapours have a penetrating odour, provoking tears, and act as powerful poisons.

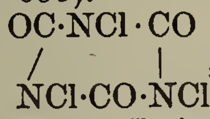
The **cyanuric halides** are converted into cyanuric acid when heated with water.

Cyanuric chloride, tricyanogen chloride, solid cyanogen chloride:



m.p. 146°, b.p. 190°, is produced (1) when liquid cyanogen chloride is kept in sealed tubes, during which polymerization 189·05 Cal. are liberated (C. 1897, I. 284). It is formed (2) directly by leading chlorine into an ethereal solution of HNC, or into anhydrous hydrocyanic acid exposed to direct sunlight (Ber. **19**, 2056), or better, by slowly dropping HNC into a saturated solution of chlorine in chloroform (Ber. **32**, 691); (3) also by the distillation of cyanuric acid, $H_3O_3N_3C_3$, with PCl_5 (Ann. **116**, 357).

When boiled with water or alkalis, it breaks up into hydrochloric and cyanuric acids (Ber. **19**, R. 599). The chlorine atoms of cyanogen chloride can be successively substituted by amino- and alkylamino-groups, whereby cyanuramine chlorides, cyanuralkylamine chlorides (p. 531), melamines, and alkyl melamines (p. 530) are formed (Ber. **32**, 693).

Trichloryl isocyanuric acid,  , m.p. 245°, is formed by the action of chlorine on potassium cyanurate. It is a nitrogen chloride, since it evolves chlorine with hydrochloric acid, and regenerates cyanuric acid with NH_3 or H_2S (C. 1902, I. 525, 804).

Cyanuric bromide, $C_3N_3Br_3$, m.p. above 300°, is produced (1) from bromocyanogen in the presence of a little bromine. (2) On heating the anhydrous bromide or its ethereal solution in sealed tubes to 130–140°. (3) By heating dry potassium ferrocyanide and also ferricyanide with bromine at 250° (Ber. **16**, 2893), or (4) on conducting HBr into the ethereal solution of CNBr (Ber. **18**, 3262). It is volatile at temperatures above 300°.

Cyanuric iodide, $C_3N_3I_3$, is produced by the action of hydriodic acid on cyanuric chloride. It is a dark-brown, insoluble powder. At 200° it readily breaks up into iodine and paracyanogen, $(CN)_n$ (Ber. **19**, 599).

Sulphur Compounds of Cyanogen, their Isomers and Polymers

The two possible structurally isomeric thiocyanic acids correspond with the two possible isomeric cyanic acids:

$HS—C{\equiv}N$ and $NH{=}C{=}S$.

Thiocyanic acid. *iso*Thiocyanic acid. Thiocarbimide.

The known thiocyanic acid and its metallic salts are constituted according to the first formula. Its salts are obtained from the cyanides by the addition of sulphur (p. 286), just as the cyanates result by the absorption of oxygen.

*iso*Thiocyanic acid, sulphocarbimide, HN : CS, and its salts are not known. Its esters (the mustard oils) do, however, exist and are isomeric with those of thiocyanic acid.

Thiocyanic acid, *sulphocyanic acid*, HS·CN, m.p. 5° (approx.), occurs in small quantities in the human stomach (Ber. **28**, 1318), and is obtained by distilling its potassium salt with dilute sulphuric acid. At 0° it forms a white crystalline mass and exercises a strongly irritating action on the mucous membranes. On melting it forms a yellow liquid which at ordinary temperatures solidifies to yellow needles accompanied by a considerable evolution of heat. It is very easily soluble in water, alcohol, and ether. The aqueous solution also precipitates polymerization products at ordinary temperatures after a short time (Ber. **40**, 3166). Free thiocyanic acid and its soluble salts colour a weakly acid solution of ferric salts a dark-red colour (C. 1901, II. 199), constituting a highly sensitive reaction, which depends on the formation of $Fe_2(CNS)_6 + 9KSNC$, when the potassium salt is employed (Ber. **22**, 2061). This reaction gives rise to the alternative name rhodanates (ῥόδον, rose), which is sometimes given to these compounds. Strong acids decompose thiocyanic acid into hydrocyanic acid and perthiocyanic acid, $C_2N_2S_3H_2$ (p. 525).

The *alkali thiocyanates* are obtained by fusing the cyanides with sulphur, just as the cyanates are formed by oxidation of the cyanides.

Potassium thiocyanate, KS·CN, crystallizes from alcohol in long, colourless prisms, which deliquesce in the air. The **sodium salt** is very deliquescent, and occurs in the saliva and urine of different animals. When heated with zinc dust it is converted into potassium cyanide (C. 1897, I. 270).

Potassium selenocyanate, KSeNC, corresponds with the thiocyanate, and is formed when potassium cyanide and selenium are melted together. It can be crystallized from alcohol. NO_2 causes the formation of *cyanogen triselenide*, $C_2N_2Se_3$, m.p. 132°, obtained as yellow leaflets from benzene solution. These substances can be used for the preparation of pure selenium (Ber. **33**, 1765).

Ammonium thiocyanate, $NH_4S{\cdot}CN$, m.p. 150°, is formed on heating hydrocyanic acid with yellow ammonium sulphide, or a solution of ammonium cyanide with sulphur. It is most readily obtained by heating CS_2 with alcoholic ammonia (*cf.* Ammonium dithiocarbamate, p. 506):

$$CS_2 + 2NH_3 \longrightarrow H_2N{\cdot}CSSNH_4 + 2NH_3 \longrightarrow NH_4S{\cdot}C \vdots N + (NH_4)_2S.$$

The salt crystallizes in prisms, which readily dissolve in water and alcohol. At 170–180° molecular transposition into thiourea occurs (similarly to ammonium cyanate, p. 495).

The salts of the heavy metals are mostly insoluble. The *mercury salt*, $Hg(CN{\cdot}S)_2$, is a grey, amorphous precipitate, which burns on ignition and swells up strongly (Pharaoh's serpents); *silver salt*, AgSNC, is a precipitate similar to silver chloride. The volumetric method of Volhard is based on its production (Ann. **190**, 1).

Thiocyanogen, $(SCN)_2$, m.p. − 3°, is obtained in solution by the action of bromine on silver thiocyanate in carbon bisulphide, and crystallizes out when the solution is cooled to − 70° (*Söderbäck*, Ann. **419**, 217). Free thiocyanogen resembles the halogens. It reacts with mercaptans with the formation of alkyl dithiocyanates, R·S·SCN, and thiocyanic acid (Ber. **55**, 1474).

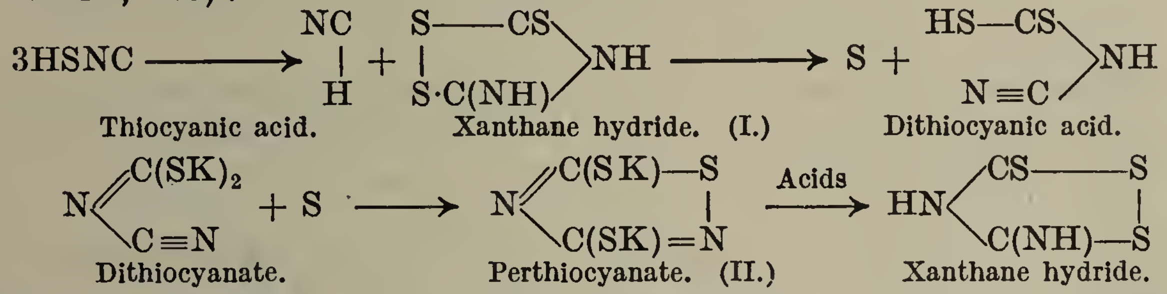
Sulphur dicyanide, thiocyanic anhydride, $(CN)_2S$, m.p. 65°, is formed when cyanogen iodide in ethereal solution acts on silver thiocyanate. It sublimes at 30°, and dissolves in water, alcohol, and ether.

Sulphur thiocyanate, $S_2(SCN)_2$, is obtained by the action of sulphur monochloride on mercury thiocyanate in organic solvents. It forms colourless crystals, m.p. − 3·3° (Ber. **55**, 1483). The compound $S(SCN)_2$ is formed from hydrogen sulphide and thiocyanogen in ethereal solution. It forms pearly crystals (Ber. **55**, 1481).

Xanthane hydride, imidothiodisulphazolidine, $C_2H_2H_2S_3$ (see formula (I) below), is prepared by decomposing a concentrated solution of thiocyanic acid, whereby hydrocyanic acid is driven off. It forms prisms soluble with difficulty in water and most other solvents.

Dithiocyanic acid, $C_2N_2H_2S_2$ = HSCS·NH·CN, is produced when alkalis act in the cold on xanthane hydride, when sulphur is thrown out and the dipotassium salt of the acid is formed. It is also prepared from cyanamide, carbon disulphide, and alcoholic potassium hydroxide. These modes of formation show the acid to be cyanamidodithiocarbonic acid, $(HS)_2C{=}NCN$ or HS_2CNHCN. The free acid consists of yellow needles, and is unstable, the potassium salt even decomposing in aqueous solution into two molecules of potassium thiocyanate; *dimethyl ester*, $(CH_3S)_2C : NCN$, m.p. 57°, is decomposed by hydrochloric acid at 200° into mercaptan, NH_3, and CO_2.

Perthiocyanic acid, $C_2N_2S_3H_2$; salts, (see formula (II) below), are formed when an alkaline solution of dithiocyanic acid is boiled with sulphur. The acid is structurally isomeric with xanthane hydride, which possesses a neutral reaction, into which it very rapidly changes in acid solution; *dimethyl ester*, $C_2N_2S(SCH_3)_2$, m.p. 42°, b.p. 279°, is decomposed by hydrochloric acid into CH_3SH, NH_4Cl, and CO_2. The following shows the connection between these peculiar reactions (Ann. **331**, 265):



Cyanogen sulphide, $(CNS)_n$, and *pseudocyanogen sulphide*, are the yellow amorphous products which result when the alkali and alkali earth thiocyanates are oxidized. Cyanogen sulphide is also formed when dry thiocyanates are treated with dry halogens, whilst *pseudo*cyanogen sulphide, which appears to be a mixture of various substances in varying proportions, is obtained from an aqueous solution of thiocyanates with halogens, nitric acid, H_2O_2, or persulphates. Cyanogen sulphide, and to a much smaller extent *pseudo*cyanogen sulphide, when treated with water or sodium hydroxide solution yields *canarine*, $C_8N_8S_7H_6O$, a yellow substantive dye for cotton (one which does not require a mordant). It possesses a weakly acid reaction. Together with canarine there is formed a yellow, non-dyeing substance, $C_3N_4H_4S_2O$, which is decomposed by alkali sulphydrates into *thioammeline*, $(CN)_3(NH_2)_2SH$, and *dithiomelanurenic acid*, *aminodithiocyanuric acid*, $(CN)_3(NH_2)(SH)_2$ (J. pr. Chem. [2] **64**, 439).

Alkyl thiocyanates, *esters of normal thiocyanic acid,* are obtained (1) by distilling potassium thiocyanate with salts of sulphuric acid ethers or with alkyl iodides:

$$KSCN + C_2H_5I = C_2H_5SCN + KI;$$

(2) by the action of CNCl on salts of the mercaptans:

$$C_2H_5SK + CNCl = C_2H_5SCN + KCl.$$

They are liquids, insoluble in water, and possessing a leek-like odour. Nascent hydrogen (zinc and sulphuric acid) converts them into hydrocyanic acid and mercaptans:

$$C_2H_5S{\cdot}CN + H_2 = HNC + C_2H_5{\cdot}SH.$$

On digesting with alcoholic potassium hydroxide, potassium thiocyanate is formed, whilst the isomeric mustard oils do not yield any potassium thiocyanate. Boiling nitric acid oxidizes them to alkylsulphonic acids (p. 175) with separation of the cyanogen group. This would prove that the alkyl group in these bodies is linked directly to sulphur.

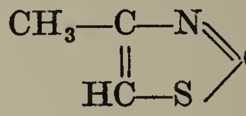
The *methyl ester* and more readily the *allyl ester* are isomerized by heating at 180–185° into the corresponding *iso*thiocyanate or mustard oil (*q.v.*) (C. 1901, II. 1115).

Methyl thiocyanate, $CH_3{\cdot}SCN$, b.p. 133°, $D_0 = 1{\cdot}080$. *Ethyl ester*, b.p. 142°, iso*propyl ester*, b.p. 152°.

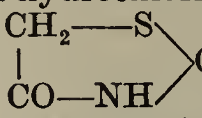
Allyl ester, $C_3H_5{\cdot}SCN$, b.p. 161°, with isomeric change into the corresponding mustard oil.

Methylene thiocyanate, $CH_2(SCN)_2$, m.p. 107° (Ber. **7**, 1282), is oxidized to methylene disulphonic acid (p. 247) (C. 1898, I. 886).

Ethylene thiocyanate, $NCS{\cdot}CH_2CH_2{\cdot}SCN$, m.p. 90° (Ber. **23**, 1083). *Ethylene selenocyanide*, m.p. 138° (Ber. **23**, 1092).

Thiocyanoacetone, $CNSCH_2\cdot CO\cdot CH_3$, $D_{20} = 1\cdot 180$, is formed from barium thiocyanate and chloroacetone (p. 265). It is a nearly colourless oil, somewhat soluble in water, and very readily soluble in ether. The alkali carbonates cause a rearrangement into oxymethylthiazole,  $\begin{matrix} CH_3—C—N \\ \| \\ HC—S \end{matrix} > C\cdot OH$ (Ber. **25**, 3648).

Thiocyanoacetic acid, $CNS\cdot CH_2CO_2H$, is formed by the action of chloroacetic acid on KCNS. It is a thick oil; *ethyl ester*, b.p. about 220°, prepared from chloroacetic ester.

On boiling the latter with concentrated hydrochloric acid, it takes up water, loses alcohol, and *iso*thiocyanoacetic acid,  $\begin{matrix} CH_2—S \\ | \\ CO—NH \end{matrix} > CO$, is formed (Ann. **249**, 27). Many of the reactions of *iso*thiocyanoacetic acid are better explained by the constitutional formula, $SCNCH_2COOH$ (or perhaps $HC \lessdot \overset{S}{\underset{N}{}} \gtrdot CHCOOH$) (*cf.* J. pr. Chem. [2] **66**, 172).

The heterocyclic bodies, derived from the products of the interaction of ammonium thiocyanate with α-chloroketones and α-chloro-fatty acids, belong to the class of *thiazoles* (Vol. II).

Mustard Oils, *Esters of* iso*Thiocyanic Acid, Alkyl Thiocarbimides.* The esters of *iso*thiocyanic acid, HN : CS, not known in a free condition, are termed mustard oils, from their most important representative. They may also be considered as sulphocarbimide derivatives.

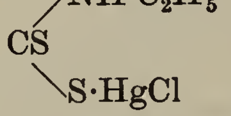
They are produced (1) by the rearrangement of the isomeric alkyl thiocyanates on the application of heat (p. 525):

$$C_3H_5SNC \longrightarrow C_3H_5NCS.$$

(2) From *primary amines*. (*a*) These combine with CS_2 in ethereal solution to form alkylammonium alkyldithiocarbamates (Ber. **23**, 282). On adding silver nitrate, mercuric chloride (Ber. **29**, R. 651) or ferric chloride (Ber. **8**, 108) to the aqueous solution of these salts, formed with primary amines, metallic compounds are first precipitated, and are decomposed by boiling into metallic sulphides, hydrogen sulphide and mustard oils.

The *mustard oil test* for the detection of primary amines (p. 195) was worked out by A. W. Hofmann.

The mechanism of the reaction is explained by Anschütz (Ann. **371**, 219) as follows:



$$CS\begin{matrix} ⁄NH\cdot C_2H_5 \\ \\ \diagdown S\cdot HgCl \end{matrix} \longrightarrow HgS + SCN\cdot C_2H_5 + HCl.$$

*iso*Thiocyanates are also obtained, together with *iso*thiouram disulphides (p. 506), by the action of iodine on the alkylammonium salts of the alkyldithiocarbamic acids.

(*b*) *iso*Thiocyanates are conveniently prepared by the action of thiocarbonyl chloride on primary amines (Rec. trav. Chim. **45**, 421):

$$CSCl_2 + NH_2\cdot R \longrightarrow SC : N\cdot R + 2HCl.$$

(3) By the action of dialkylthioureas (p. 509) with phosphorus pentoxide (Ber. **14**, 985).

(4) From *iso*cyanic esters and P_2S_5 (Ber. **18**, R. 72).

Properties.—The mustard oils are liquids, almost insoluble in water, and possess a very penetrating odour, which provokes tears. They boil at lower temperatures than the isomeric thiocyanic esters.

Reactions.—(1) When heated with hydrochloric acid to 100°, or with H_2O to 200°, they break up into primary amines, hydrogen sulphide, and carbon dioxide (C. 1899, I. 885):

$$C_2H_5NCS + 2H_2O = C_2H_5NH_2 + CO_2 + H_2S.$$

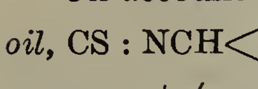
(2) When heated with a little dilute sulphuric acid, carbon oxysulphide, COS, is formed, together with the amine. (3) When heated with carboxylic acids they yield alkylated acid amides and COS; and (4) with carboxylic anhydrides, diacidyl amides and COS (Ber. **26,** 2648). (5) Nascent hydrogen (zinc and hydrochloric acid) converts them into thioformaldehyde (p. 246) and primary amines:

$$C_2H_5NCS + 2H_2 = CSH_2 + C_2H_5NH_2.$$

(6) When the mustard oils are heated with absolute alcohol to 100°, or with alcoholic potassium hydroxide, they pass into sulphourethanes. (7) They unite with ammonia and amines, yielding alkyl thioureas (*q.v.*). (8) Upon boiling their alcoholic solution with HgO or $HgCl_2$, a substitution of oxygen for sulphur occurs, with formation of esters of *iso*cyanic acid, which immediately yield the dialkylureas when treated with water (see p. 519). (9) Consult Ann. **285,** 154, for the action of the halogens on the mustard oils.

Methyl iso*thiocyanate,* CH_3NCS, m.p. 34°, b.p. 119°.

Ethyl ester, b.p. 133°, $D_0 = 1{\cdot}019$. *Propyl ester,* b.p. 153°. iso*Propyl ester,* b.p. 137°. n.-*Butyl ester,* b.p. 167°. iso*Butyl ester,* b.p. 162°. tert.-*Butyl ester,* b.p. 142°. n.-*Hexyl ester,* b.p. 212°. *Heptyl ester,* b.p. 238° (Ber. **29,** R. 651). sec.-*Octyl ester,* b.p. 232°.

On account of its occurrence the following is noteworthy: sec.-*butyl mustard oil,*  $CS:NCH\begin{smallmatrix}C_2H_5\\CH_3\end{smallmatrix}$, b.p. 159·5°, $D_{12} = 0{\cdot}944$, is found in the ethereal oils of spoonwort (or scurvy grass) (*Cochlearia officinalis*); it is dextro-rotatory to polarized light, and on decomposition gives a dextro-rotatory *sec.*-butylamine (C. 1901, II. 29).

The most important of the mustard oils is the common or—

Allyl mustard oil, *allyl* iso*thiocyanate,* $C_3H_5N:CS$, b.p. 150·7°, $D_{10} = 1{\cdot}017$, the principal constituent of ordinary mustard oil, is obtained by distilling powdered black mustard seeds (*Sinapis nigra*), or radish oil from *Cochlearia armoracia,* with water. Mustard seeds contain potassium myronate (see *Glucosides,* Vol. II), which in the presence of water, under the influence of a ferment, *myrosin* (also present in the seed), breaks up into dextrose, potassium hydrogen sulphate, and mustard oil.

The reaction occurs even at 0°, and a small amount of allyl thiocyanate is produced at the same time:

$$C_{10}H_{18}KNO_{10}S_2 = C_6H_{12}O_6 + KHSO_4 + C_3H_5NCS.$$

Mustard oil is artificially prepared by distilling allyl iodide or bromide with alcoholic potassium or silver thiocyanate, the first-formed allyl thiocyanate undergoing isomeric change (*Gerlich,* Ann. **178,** 80: C. 1906, II. 1063):

$$KSCN + C_3H_5I = C_3N_5NCS + KI;$$

a molecular rearrangement occurs here.

Pure allyl mustard oil is a liquid not readily dissolved by water. It has a pungent odour and causes blisters upon the skin. When heated with water or hydrochloric acid the following reaction ensues:

$$C_3H_5NCS + 2H_2O = CO_2 + H_2S + C_3H_5NH_2.$$

It unites with aqueous ammonia to form allylthiourea (p. 509). When heated with water and lead oxide it yields diallylurea (p. 497).

Acyl thiocarbimides, or **acyl *iso*thiocyanates,** are produced by the action of fatty-acid chlorides, dissolved in benzene, on lead thiocyanate. *Acetyl thiocarbimide,* $CH_3CO(NCS)$, *valeryl thiocarbimide,* $C_4H_9CO{\cdot}NCS$ (Ber. **29**, R. 85), and *carbethoxyl thiocarbimide,* $C_2H_5OCO{\cdot}NCS$, b.p. 66°/21 mm. (Ber. **29**, R. 514), were obtained in this manner. Amines combine with them to form either alkylamides, AcNHR, and amine thiocyanates, $R{\cdot}NH_2$, HSCN, or acylalkylthioureas, AcNHCSNHR (C. 1905, I. 1098: 1906, II. 773, etc.).

Thiocyanuric acid, $(HS)_3C_3N_3$, corresponds with cyanuric acid. *iso*Thiocyanuric acid is unknown, like *iso*cyanuric acid. Thiocyanuric acid results from cyanuric chloride (p. 523) and potassium hydrosulphide. It consists of small yellow needles, which decompose but do not melt above 200°.

Its *esters* result when cyanuric chloride and sodium mercaptides interact, and by the polymerization of the thiocyanic esters, $RS{\cdot}CN$, when heated to 180° with a little HCl. More HCl causes them to split up into cyanuric acid and mercaptans.

Methyl ester, $(CH_3S)_3C_3N_3$, m.p. 188°, yields melamine with ammonia (p. 530) (Ber. **18**, 2755). *Monothiocyanuric dimethyl ester,* $(SH)(OCH_3)_2C_3N_3$, is prepared from *O*-dimethylcyanuric chloride (p. 521) and KSH. When hydrolysed with HCl, it yields *monothiocyanuric acid,* $(HS)(HO)_2C_3N_3$, which gives a characteristic mercury salt (Ber. **36**, 3196).

iso*Thiocyanuric esters,* $(RN)_3C_3S_3$, appear to have been formed by the polymerization of mustard oils with potassium acetate (Ber. **25**, 876).

Cyanamide and the Amides of Cyanuric Acid

Cyanamide, $CN{\cdot}NH_2$, m.p. 40°, the nitrile of carbamic acid, frequently reacts also according to the carbodiimide formula, $HN:C:NH$.

It is formed (1) by the action of chloro- or bromo-cyanogen on an ethereal or aqueous solution of ammonia (*Bineau,* 1838; *Cloez* and *Cannizzaro,* 1851):

$$CNCl + 2NH_3 = CN{\cdot}NH_2 + NH_4Cl;$$

and also (2) by the desulphurizing of thiourea by means of mercuric chloride, lead peroxide, or mercuric oxide (Ber. **18**, 461: Ann. **331**, 282); or lead hydroxide in presence of alkalis (C. 1897, I. 367):

$$CS(NH_2)_2 + HgO = CN_2H_2 + HgS + H_2O.$$

(3) By treating urea with thionyl chloride:

$$CO(NH_2)_2 + SOCl_2 = CN_2H_2 + SO_2 + 2HCl.$$

(4) Metallic derivatives of cyanamide with sodium, calcium, etc., are prepared on a technical scale, and yield cyanamide when decomposed with acids. Preparation of cyanamide from its calcium derivative, see J. Biol. Chem. **32**, 297.

(*a*) Sodium amide and carbon or carbon compounds heated to 400–600° produce sodium cyanamide (C. 1905, II. 1650, etc.):

$$2NH_2Na + C \xrightarrow{\qquad} CN_2Na_2 + 4H.$$

At 600° another atom of carbon enters into reaction and sodium cyanide, NaNC, is produced (C. 1904, I. 64).

(*b*) Calcium carbide, mixed with certain substances such as calcium chloride, and when heated to high temperatures, absorbs nitrogen and is converted into calcium cyanamide (C. 1905, II. 1059 : Ber. **40**, 310, etc. :

$$C_2Ca + N_2 \longrightarrow CN_2Ca + C.$$

(*c*) Carbonates, such as those of barium and lead, react with ammonia at temperatures of incandescence, yielding metallic cyanamides (C. 1913, I. 677) :

$$PbCO_3 + 2NH_3 \longrightarrow CN_2Pb + 3H_2O.$$

Cyanamide forms colourless, very hygroscopic crystals, m.p. 41–42°, b.p. 134–144°/18 mm. It is easily soluble in water, alcohol, and ether. If heated it polymerizes to dicyandiamide and tricyantriamide (melamine).

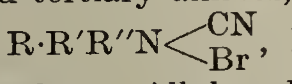
Salts.—It forms salts with strong acids, but these are decomposed by water. It also forms salts with metals. An ammoniacal silver nitrate solution throws down a yellow precipitate, $CN{\cdot}NAg_2$, from its solutions.

Reactions.—(1) By the action of sulphuric acid or hydrochloric acid, it absorbs water and yields urea (p. 494). (2) H_2S converts it into thiourea (p. 508), and (3) NH_3 into guanidine (p. 512), whilst substituted guanidines are produced upon introducing the hydrochlorides of primary amines. (4) Alcohols and hydrochloric acid change cyanamide into ethers of *iso*thiourea (p. 510).

Mono-alkyl cyanamides are obtained (1) by the action of cyanogen chloride on primary amines in ethereal solution, or from aqueous solutions of amines and potassium cyanide with bromine (C. 1906, II. 1046) ; (2) by heating alkyl thioureas with mercuric oxide and water.

Methylcyanamide, $CN{\cdot}NHCH_3$, and *ethylcyanamide*, $CN{\cdot}NHC_2H_5$, are noncrystallizable, thick syrups with neutral reaction. They are readily converted into polymeric *iso*melamine derivatives.

Allylcyanamide, $CN{\cdot}NHC_3H_5$, (*sinamine*) is obtained from allyl thiourea. It is crystalline and polymerizes readily into triallyl melamine.

Dialkyl cyanamides are formed (1) from CNBr, or KCN + Br (C. 1906, II. 1046) and sec.-bases ; (2) from silver cyanamide, $CN{\cdot}NAg_2$, and alkyl iodides. (3) From CNBr and tertiary amines, whereby the first-formed trialkylcyanammonium bromide,  $R{\cdot}R'R''N{<}\begin{smallmatrix}CN\\Br\end{smallmatrix}$, loses alkyl bromide—the smallest of the alkyl radicals being lost. Allyl and benzyl radicals, however, behave exceptionally, and are split off even more easily than the methyl group (Ber. **35**, 1279). On the use of these methods for breaking down tertiary cyclic amines, see Ber. **40**, 3914.

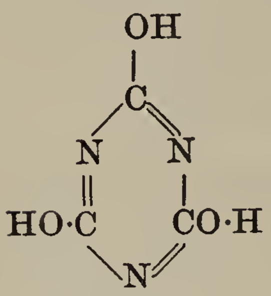
Dimethylcyanamide, cyanodimethylamine, $CN{\cdot}N(CH_3)_2$, b.p. 68°/10 mm. ; *diethylcyanamide*, $CN{\cdot}N(C_2H_5)_2$, b.p. 188°, is decomposed, when boiled with hydrochloric acid, into CO_2, NH_3 and diethylamine, $NH(C_2H_5)_2$. *Dipropylcyanamide*, b.p. 89°/15 mm. *Diamylcyanamide*, b.p. 130°/10 mm. Treated with ammonia and sulphuretted hydrogen in alcoholic solution, the cyanodialkylamines are easily converted into the corresponding thioureas (Ber. **32**, 1872).

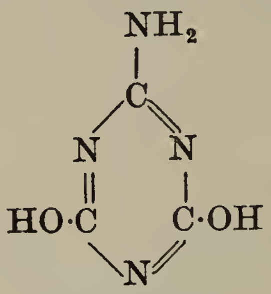
An example of a dialkyl-substituted carbodiimide is *di-*n*-propylcarbodiimide*, $C(=N{\cdot}C_3H_7)_2$, b.p. 177°, which is produced from *sym.*-dipropylthiourea and HgO (Ber. **26**, R. 189).

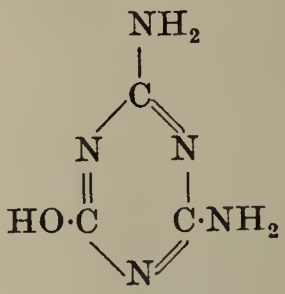
For the conversion of cyanamide into cyanamidocarbonic acid, cyanamidodicarbonic acid, cyanamidodithiocarbonic acid, see pp. 502, 525.

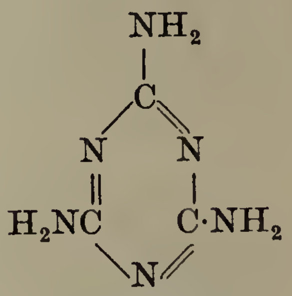
Amides of Cyanuric Acid and Imides of *iso*Cyanuric Acid

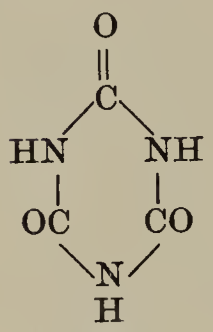
Three amides are derived from cyanuric acid, and three tautomeric imides from the hypothetical *iso*cyanuric acid :

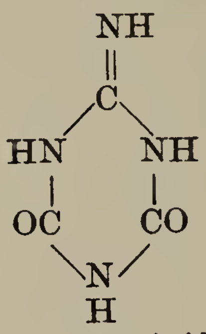

Normal cyanuric acid.

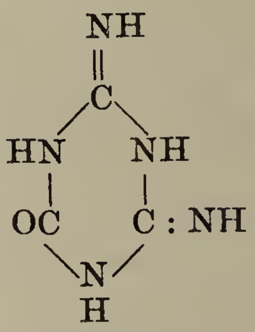

Cyanuromonamide. Ammelide.

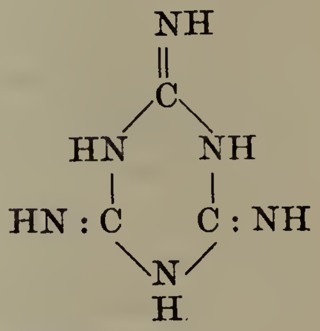

Cyanurodiamide. Ammeline.


Cyanurotriamide. Melamine.


*iso*Cyanuric acid.


*iso*Cyanuromonimide.


*iso*Cyanurodiimide. *iso*Ammeline.


*iso*Cyanurotriimide. *iso*Melamine.

Melamine, *cyanuramide,* $C_3N_3(NH_2)_3$, is obtained (1) as thiocyanate, by the rapid heating of ammonium thiocyanate (Ber. **19**, R. 340), together with *melam* and *melem* (see below) ; (2) the polymerization of cyanamide or dicyandiamide on heating to 150° (together with melam) ; (3) by heating methyl trithiocyanuric ester to 180° with concentrated ammonia ; and (4) by heating cyanuric chloride to 100° with concentrated ammonia (Ber. **18**, 2765) :

$$C_3N_3Cl_3 + 6NH_3 = C_3N_3(NH_2)_3 + 3NH_4Cl.$$

Melamine is nearly insoluble in alcohol and ether. It crystallizes from hot water in shining monoclinic prisms. It sublimes on heating and decomposes into mellon and NH_2. It forms crystalline salts with 1 equivalent of acid. Fusion with potassium hydroxide converts it into potassium cyanate.

On boiling with alkalis or acids melamine splits off ammonia and passes successively into *ammeline,* $C_3H_5N_5O = C_3N_3(NH_2)_2{\cdot}OH$, a white powder insoluble in water, but soluble in alkalis and mineral acids (Ber. **21**, R. 789) ; *ammelide, melanurenic acid,* $C_3H_4N_4O_2 = C_3N_3(NH_2)(OH)_2$, a white powder which forms salts with both acids and bases, and finally into cyanuric acid, $C_3N_3(OH)_3$ (Ber. **19**, R. 341).

Melanurenic acid is also formed from melam and melem (see below), when heated with concentrated H_2SO_4 (Ber. **19**, R. 341 : **18**, 3106).

Melam, $C_6H_9N_{11} = [(NH_2)_2C_3N_3]_2NH$ (?), *melem,* $C_6H_6N_{10} = [(NH_2)C_3N_3(NH)]_2$ (?), and *mellon,* $C_6H_3N_9 = C_3N_3(NH)_3C_3N_3$ (?), are formed by heating ammonium thiocyanate, the first two at 200°, and the last at red heat. They are amorphous white substances (Ber. **19**, R. 340).

Alkyl Derivatives of the Melamines.

Whilst melamine is only known in one form, as cyanurotriamide, two series of isomeric alkyl derivatives exist—derived from normal melamine and the hypothetical *iso*melamine :

(1) $C_3N_3(NHR')_3$ and $C_3N_3(NR'_2)_3$. Normal alkyl melamines.

(2) $C_3N_3H_3(NR')_3$. Alkyl*iso*melamines.

These are distinguished from each other not only by the manner of their preparation, but also by their reactions.

(1) **Normal alkyl melamines** are obtained from the trithiocyanuric esters, $C_3N_3(S{\cdot}CH_3)_3$, and from cyanuric chloride, $C_3N_3Cl_3$, upon heating with primary and secondary amines (Ber. **18**, R. 498) :

$$C_3N_3Cl_3 + 3NH(CH_3)_2 = C_3N_3[N(CH_3)_2]_3.$$

Heating with concentrated hydrochloric acid causes them to split up into cyanuric acid and the constituent alkylamines.

Trimethylmelamine, $C_3N_3(NH{\cdot}CH_3)_3$, m.p. 130°, dissolves readily in water, alcohol and ether. *Triethylmelamine*, $C_3N_3(NH{\cdot}C_2H_5)_3$, crystallizes in needles, m.p. 74°.

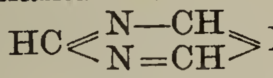
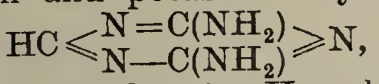
Methylethylmelamine, $C_3H_3(NHC_2H_5)(NHCH_3)NH_2$, m.p. 176°, is prepared from cyanuric chloride by the successive substitution of NH_2-, CH_3NH-, and C_2H_5NH- groups, it being immaterial in which order the groups are introduced. (See p. 523.)

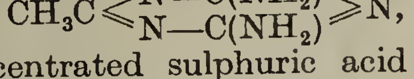
Hexamethylmelamine, $C_3N_3[N(CH_3)_2]_3$, m.p. 171°, *hexaethylmelamine*, $C_3N_3[N(C_2H_5)_2]_3$, is a liquid, which is decomposed by hydrochloric acid into cyanuric acid and 3 molecules of diethylamine.

(2) **Alkyl *iso*melamines** are formed by the polymerization of the alkyl cyanamides, $CN{\cdot}NHR'$ (p. 529), upon evaporating their solutions, obtained from the alkyl thioureas on warming with mercuric oxide and water. They are crystalline bodies. When heated with hydrochloric acid they yield cyanuric esters and ammonium chloride (Ber. **18**, 2784).

Trimethyl iso*melamine*, $C_3N_3(CH_3)_3(NH)_3 + 3H_2O$, m.p. 179°, anhydrous. It already sublimes at about 100°. *Triethyl* iso*melamine*, $C_3N_3(C_2H_5)_3(NH)_3 + 4H_2O$, consists of very soluble needles. See Ber. **18**, 3217, for the phenyl derivatives of the mixed melamines (also amide and imide bodies).

Cyanuramine Chlorides.—*Cyanuramine dichloride*, $C_3N_3Cl_2(NH_2)$, corresponds with cyanuric monamide or ammelide (p. 530) or melanurenic acid; and *cyanurodiamine monochloride*, $C_3N_3Cl(NH_2)_2$, with cyanuric diamide or ammeline. The former substance is formed by the action of ammonia on an ethereal solution of cyanuric chloride; the latter by aqueous ammonia on the chloride. Similar conditions of experiment applied to methylamine and ethylamine give rise to the following substances: *cyanuromethylamino dichloride*, $C_3N_3Cl_2(NHCH_3)$, m.p. 161°; *cyanuroethylamino dichloride*, $C_3N_3Cl_2(NHC_2H_5)_2$, m.p. 107°; *cyanuroaminomethylamino chloride*, $C_3N_3Cl(NH_2)(NHCH_3)$; *cyanuroaminoethylamino chloride*, $C_3N_3ClNH(C_2H_5)(NH_2)$, m.p. 176°; *cyanuromethylaminoethylamino chloride*, $C_3H_3Cl(NHCH_3)(NHC_2H_5)$, m.p. 235°. Ethylamine, methylamine and ammonia convert the three last-named chlorides into methyl ethyl melamine.

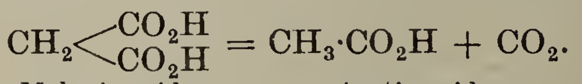
Cyanuramine Hydrides, Guanamines.—The hydrogen compound, *hydrocyanuric acid* or *trihydrocyanic acid*,  $HC{<}{\begin{matrix}N{-}CH\\N{=}CH\end{matrix}}{>}N$, corresponding with cyanuric chloride, is unknown. However, reduction of cyanuramine dichloride forms *monaminohydrocyanuric acid*, $C_3N_3H_2{\cdot}NH_2$, m.p. 225°, whilst cyanodiamine monochloride yields diaminohydrocyanuric acid. *Guanamines* are the bases formed when fatty-acid guanidine salts are heated to 220°–230°, whereby water and ammonia are driven off (*Nencki*, Ber. **9**, 228). The simplest guanamine is formed when guanidine formate is heated, or when biguanide (p. 515) is acted on by chloroform and potassium hydroxide solution (Ber. **25**, 535). This *formoguanamine*,  $HC{<}{\begin{matrix}N{=}C(NH_2)\\N{-}C(NH_2)\end{matrix}}{>}N$, m.p. 325°, is identical with diaminohydrocyanuric acid (see above). Homologous guanamines are derived from this, by the replacement of the H-atoms in the CH- group by alcohol radicals.

Acetoguanamine,  $CH_3C{<}{\begin{matrix}N{=}C(NH_2)\\N{-}C(NH_2)\end{matrix}}{>}N$, m.p. 265°, is produced from guanidine acetate. Concentrated sulphuric acid at 150° converts it into acetoguanamide (*cf.* Acetyl urethane, p. 491).

10. DIBASIC ACIDS, DICARBOXYLIC ACIDS

A. PARAFFIN DICARBOXYLIC ACIDS, OXALIC ACID SERIES, $C_nH_{2n-2}O_4$, $C_nH_{2n}(CO_2H)_2$

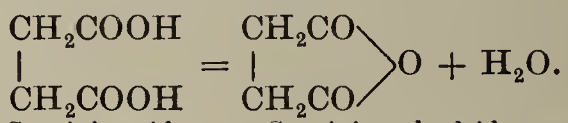
The acids of this series contain two carboxyl groups, and are therefore dibasic. They differ very markedly from each other on the application of heat, depending upon the relative positions of the carboxyl groups. Oxalic acid, $CO_2H{\cdot}CO_2H$, the first member of the series, breaks down on heating chiefly into CO_2, CO and water, but in part into CO_2 and formic acid. The latter decomposition is characteristic of all dibasic acids, in which the two carboxyls are attached to the same carbon atom—the β-dicarboxylic acids, *e.g.* malonic acid, $CH_2(CO_2H)_2$. The latter acid and all mono- and di-alkylmalonic acids decompose on heating at the ordinary pressure into acetic acid, and mono- and di-alkylacetic acids with the elimination of CO_2:



$$CH_2{<}\begin{matrix}CO_2H\\ CO_2H\end{matrix} = CH_3{\cdot}CO_2H + CO_2.$$

Malonic acid. Acetic acid.

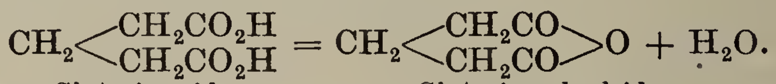
On the other hand, when the two carboxyl groups are attached to adjacent carbon atoms, as in ordinary succinic acid, $CO_2H{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$, and in the alkylsuccinic acids, these dicarboxylic acids, when heated, do not give up CO_2, but part with water and pass into anhydrides, which can also be prepared in other ways, whereas the simple anhydrides of the malonic acids are not known (p. 543). Succinic acid is the type of these acids:



$$\begin{matrix}CH_2COOH\\ |\\ CH_2COOH\end{matrix} = \begin{matrix}CH_2CO\\ |\\ CH_2CO\end{matrix}{>}O + H_2O.$$

Succinic acid. Succinic anhydride.

Glutaric acid, or normal pyrotartaric acid, $CO_2H{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$, in which the two carboxyl groups are attached to two carbon atoms, separated by a third, behaves in this manner. Like succinic acid, it yields a corresponding anhydride when it is heated. All alkylglutaric acids behave analogously:



$$CH_2{<}\begin{matrix}CH_2CO_2H\\ CH_2CO_2H\end{matrix} = CH_2{<}\begin{matrix}CH_2CO\\ CH_2CO\end{matrix}{>}O + H_2O.$$

Glutaric acid. Glutaric anhydride.

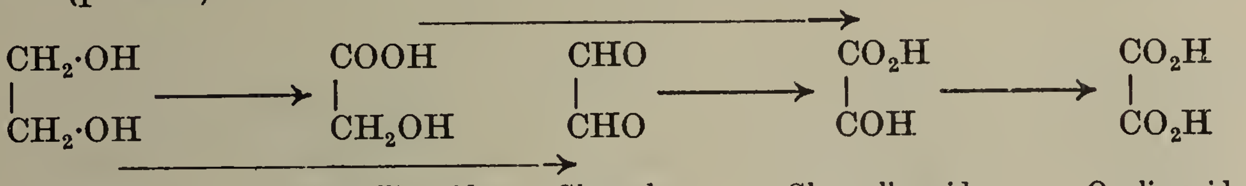
Differentiation of succinic and glutaric derivatives, see *Windaus*, Ber. **54**, 581.

When the two carboxyl groups are separated by four or more carbon atoms, they do not interact on the application of heat, and adipic acid, $COOH{\cdot}[CH_2]_4{\cdot}COOH$, for example, volatilizes without decomposition. Cyclic ketones, however, can be obtained from these higher dicarboxylic acids, by distillation of certain salts, notably the thorium salt (see p. 560), or by heating the acids with acetic anhydride (*Blanc*, Compt. rend. **144**, 1356).

These acids are frequently obtained by the oxidation of natural ring compounds, and owing to their different behaviour on heating, the number of carbon atoms in the ring by the breakdown of which they are formed can be deduced (*Blanc, loc. cit.*). This method has been much used by Windaus and Wieland in the determination of the constitutions of the sterols and bile acids.

Formation.—The most important general methods are—

(1) Oxidation of (*a*) diprimary glycols, (*b*) primary hydroxy-aldehydes, (*c*) dialdehydes, (*d*) primary hydroxy-acids, and (*e*) aldehyde acids (p. 455):

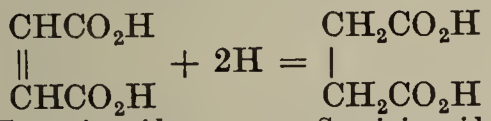


$$\begin{array}{c}CH_2\cdot OH\\|\\CH_2\cdot OH\end{array}\longrightarrow\begin{array}{c}COOH\\|\\CH_2OH\end{array}\quad\begin{array}{c}CHO\\|\\CHO\end{array}\longrightarrow\begin{array}{c}CO_2H\\|\\COH\end{array}\longrightarrow\begin{array}{c}CO_2H\\|\\CO_2H\end{array}$$

Glycol. Glycollic acid. Glyoxal. Glyoxylic acid. Oxalic acid.

The dibasic acids are also formed when the fatty acids, $C_nH_{2n}O_2$, and the acids of the oleic acid series, as well as the fats, are oxidized by nitric acid. Certain hydrocarbons, C_nH_{2n}, have also been converted into dibasic acids by the action of potassium permanganate.

(2) By the reduction of unsaturated dicarboxylic acids:



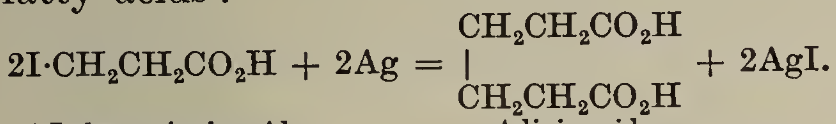
$$\begin{array}{c}CHCO_2H\\||\\CHCO_2H\end{array}+2H=\begin{array}{c}CH_2CO_2H\\|\\CH_2CO_2H\end{array}$$

Fumaric acid. Succinic acid.

(3) When hydroxydicarboxylic acids and halogen dicarboxylic acids are reduced.

Nucleus-synthetic Methods of Formation.—These are very numerous.

(4) When silver in powder form (Ber. **2**, 720) acts on mono-iodo (or bromo-) fatty acids:

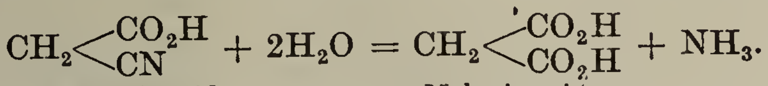


$$2I\cdot CH_2CH_2CO_2H+2Ag=\begin{array}{c}CH_2CH_2CO_2H\\|\\CH_2CH_2CO_2H\end{array}+2AgI.$$

β-Iodopropionic acid. Adipic acid.

Trimethylglutaric acid is formed as well as tetramethylsuccinic acid by the action of silver on α-bromo*iso*butyric acid (see p. 558).

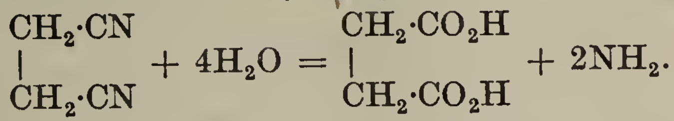
(5*a*) Conversion of monohalogen substituted fatty acids into cyano-derivatives, and boiling the latter with alkalis or acids (pp. 297 and 324):



$$CH_2{<}{\begin{array}{l}CO_2H\\CN\end{array}}+2H_2O=CH_2{<}{\begin{array}{l}CO_2H\\CO_2H\end{array}}+NH_3.$$

Cyanoacetic acid. Malonic acid.

(5*b*) Conversion of the halogen addition products of the olefines, C_nH_{2n}, into cyanides and the hydrolysis of the latter:



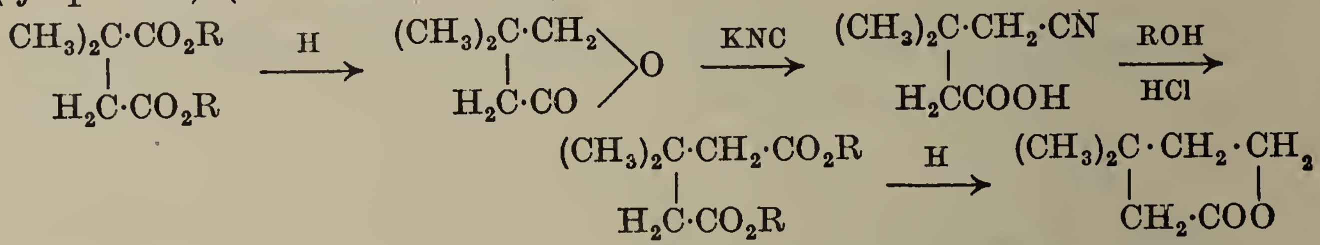
$$\begin{array}{c}CH_2\cdot CN\\|\\CH_2\cdot CN\end{array}+4H_2O=\begin{array}{c}CH_2\cdot CO_2H\\|\\CH_2\cdot CO_2H\end{array}+2NH_2.$$

Only the halogen products having their halogen atoms attached to two different carbon atoms can be converted into dicyanides.

Since dicarboxylic acids or their esters or anhydrides can be reduced to hydroxycarboxylic acids or their lactones (p. 424) by means of nascent hydrogen (from sodium and alcohol, electrolysis, etc.), and these can be converted into cyanocarboxylic acids, *via* halogen-carboxylic acids, it follows that these processes provide a means for the synthesis of progressively higher members of the dicarboxylic acid series :

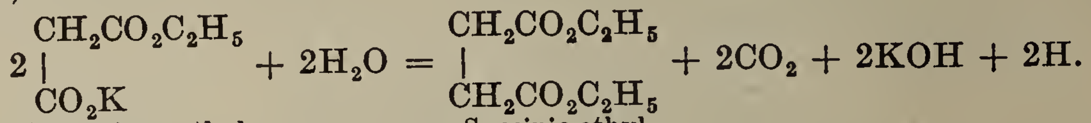
$$CO_2H{\cdot}CO_2H \longrightarrow CH_2OH{\cdot}CO_2H \longrightarrow CH_2ClCO_2H \longrightarrow CN{\cdot}CH_2CO_2H \longrightarrow CO_2H{\cdot}CH_2CO_2H.$$

(5*c*) γ- and δ-Lactones, when heated with potassium cyanide and subsequently hydrolysed, are converted directly into a higher acid (*cf*. p. 561) (C. 1905, II. 755) :



(6) Mono- and di-alkyl malonic acids can be synthesized by direct replacement of the hydrogen atoms of the CH_2 group of the malonic esters by alkyl groups, as in the case of acetoacetic ester (p. 471). This reaction will be more fully developed under malonic acid (p. 545).

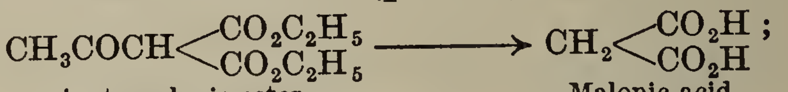
(7) By the electrolysis of concentrated solutions of the potassium salts of the dicarboxylic acid mono-alkyl esters (see electrolysis of the mono-carboxylic acids (pp. 94, 298) (see Proc. Roy. Soc. Edin. **46**, 71) :



$$2\begin{array}{l}CH_2CO_2C_2H_5\\ |\\ CO_2K\end{array} + 2H_2O = \begin{array}{l}CH_2CO_2C_2H_5\\ |\\ CH_2CO_2C_2H_5\end{array} + 2CO_2 + 2KOH + 2H.$$

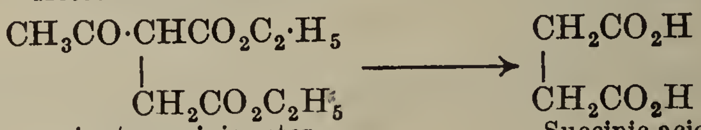
Potassium ethyl malonate. Succinic ethyl ester.

(8) A very general method for the synthesis of dibasic acids is based upon the decomposition of β-ketonedicarboxylic esters. Acid radicals are introduced into the latter and the products decomposed by concentrated alkali solutions (p. 624) :



$$CH_3COCH<\begin{array}{l}CO_2C_2H_5\\ CO_2C_2H_5\end{array} \longrightarrow CH_2<\begin{array}{l}CO_2H\\ CO_2H\end{array};$$

Acetomalonic ester. Malonic acid.



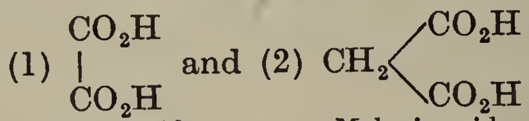
$$\begin{array}{l}CH_3CO{\cdot}CHCO_2C_2{\cdot}H_5\\ \quad |\\ \quad CH_2CO_2C_2H_5\end{array} \longrightarrow \begin{array}{l}CH_2CO_2H\\ |\\ CH_2CO_2H\end{array}$$

Acetosuccinic ester. Succinic acid.

(9) Tricarboxylic acids, which contain two carboxyl groups attached to the same C-atom, split off CO_2 and yield the dibasic acids. Ethanetricarboxylic acid yields succinic acid, and *iso*butanetricarboxylic acid gives rise to *unsym.*-dimethyl succinic acid, etc.

(10) General method for preparation of the higher polymethylene dicarboxylic acids, see p. 562.

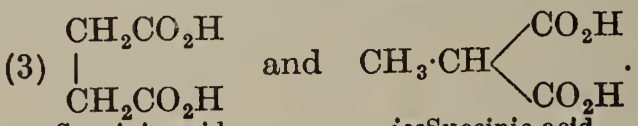
Isomerism.—Isomers of the first two members of the series—



$$(1)\ \begin{array}{l}CO_2H\\ |\\ CO_2H\end{array} \text{ and } (2)\ CH_2<\begin{array}{l}CO_2H\\ CO_2H\end{array}$$

Oxalic acid. Malonic acid.

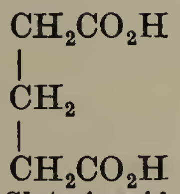
are not possible. For the third member two isomers exist :



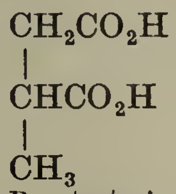
$$(3)\ \begin{array}{l}CH_2CO_2H\\ |\\ CH_2CO_2H\end{array} \text{ and } CH_3{\cdot}CH<\begin{array}{l}CO_2H\\ CO_2H\end{array}.$$

Succinic acid. *iso*Succinic acid (methylmalonic acid).

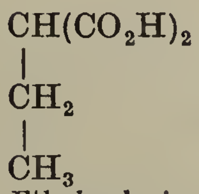
There are four possible isomers with the formula $C_3H_8\begin{smallmatrix}\diagup CO_2H \\ \diagdown CO_2H\end{smallmatrix}$, etc.; all are known:

(4) 
$\begin{array}{l} CH_2CO_2H \\ | \\ CH_2 \\ | \\ CH_2CO_2H \end{array}$

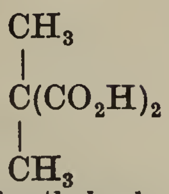
Glutaric acid.


$\begin{array}{l} CH_2CO_2H \\ | \\ CHCO_2H \\ | \\ CH_3 \end{array}$

Pyrotartaric acid.


$\begin{array}{l} CH(CO_2H)_2 \\ | \\ CH_2 \\ | \\ CH_3 \end{array}$

Ethylmalonic acid.


$\begin{array}{l} CH_3 \\ | \\ C(CO_2H)_2 \\ | \\ CH_3 \end{array}$

Dimethylmalonic acid.

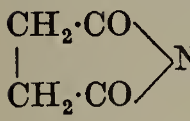
(5) The fifth member of the series, the acid $C_4H_8(CO_2H)_2$, has nine possible isomers; all are known.

(6) There are twenty-four imaginable isomers of the sixth member—the acids $C_5H_{10}(CO_2H)_2$ (Ann. **292**, 134).

Nomenclature.—The names of the older dicarboxylic acids—*e.g.* oxalic, malonic, succinic, etc.—recall the occurrence or the methods of making these acids. Many acids are described as substitution products of the polymethylene carboxylic acids, $COOH(CH_2)_n\cdot COOH$, *e.g.* methylsuccinic acid, $COOH\cdot CH_2\cdot CH(CH_3)\cdot COOH$, etc.

The "Geneva" names are deduced, like those for the mono-carboxylic acids, from the corresponding hydrocarbons; oxalic acid = [ethane-diacid]; malonic acid = [propane-diacid]; succinic acid = [butane-diacid]. The bivalent residues linked to the two hydroxyls are called the radicals of the dicarboxylic acids —*e.g.* $CO\cdot CO$, oxalyl; $CO\cdot CH_2\cdot CO$, malonyl, and $CO\cdot CH_2\cdot CH_2\cdot CO$, succinyl. The melting points of the normal dicarboxylic acids exhibit a regularity; the members containing an even number of carbon atoms melt higher than those with an odd number (Baeyer).

Derivatives of the Dicarboxylic Acids.—It has been indicated in connection with the monocarboxylic acids (p. 278) what derivatives of an acid can be obtained by a change in the carboxyl group. As might well be expected, the derivatives of the dicarboxylic acids are much more numerous, because not only the one group, but both carboxyls can take part in the reaction. The heterocyclic derivatives of the succinic and glutaric acid groups are particularly noteworthy: they are the *anhydrides* (p. 551) and the *acid imides*, *e.g. succinimide*,


$\begin{array}{l} CH_2\cdot CO \\ | \\ CH_2\cdot CO \end{array}\!\!>NH$, and *glutarimide*, $CH_2\begin{smallmatrix}\diagup CH_2\cdot CO \diagdown \\ \diagdown CH_2\cdot CO \diagup\end{smallmatrix}NH$ (p. 552).

Oxalic Acid and its Derivatives

(1) **Oxalic acid,** [ethane-diacid], $C_2O_4H_2$, occurs in many plants, chiefly as potassium salt in the different varieties of *Oxalis* and *Rumex*. The calcium salt is often found crystallized in plant cells; it constitutes the chief ingredient of certain calculi.

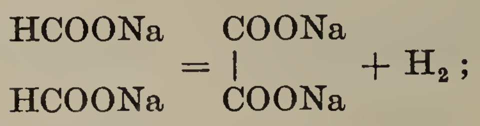
The acid may be prepared artificially (1) by *oxidation of* many carbon compounds, such as sugar, starch, etc., with nitric acid.

Frequent mention has been made of its formation in the oxidation of glycol, glyoxal, glycollic acid and glyoxylic acid.

(2) From *cellulose*: by fusing sawdust with potassium hydroxide in iron pans at 200–220°. The fused mass is extracted with water, precipitated as calcium oxalate, and this is then decomposed by sulphuric acid (technical method).

(3) It is formed *synthetically* (*a*) by rapidly heating sodium formate above 440° (Ber. **15**, 4507): the addition of sodium hydroxide, car-

bonates or oxalates enable the reaction to take place at 360°, and more completely (C. 1903, II. 777: 1905, II. 367):



$$\begin{matrix}HCOONa\\HCOONa\end{matrix} = \begin{matrix}COONa\\|\\COONa\end{matrix} + H_2;$$

This method is used technically.

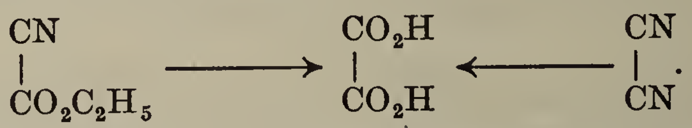
(*b*) by oxidizing formic acid with nitric acid (Ber. **17**, 9).

(4) By conducting *carbon dioxide* over metallic sodium heated to 350–360° (Ann. **146**, 140):

$$2CO_2 + Na_2 = C_2O_4Na_2.$$

CO_2 and potassium hydride yield a mixture of potassium formate (p. 282) and oxalate.

(5) Upon treating its *nitriles*, cyanoformic ester and cyanogen, with hydrochloric acid or water:



$$\begin{matrix}CN\\|\\CO_2C_2H_5\end{matrix} \longrightarrow \begin{matrix}CO_2H\\|\\CO_2H\end{matrix} \longleftarrow \begin{matrix}CN\\|\\CN\end{matrix}.$$

History.—At the beginning of the seventeenth century salt of sorrel was known, and was considered to be a variety of argol. *Wiegleb* (1778) recognized the peculiarity of the acid contained in it. *Scheele* had obtained free oxalic acid as early as 1776 by oxidizing sugar with nitric acid, and showed in 1784 that it was identical with the acid of the salt of sorrel. *Gay-Lussac* (1829) discovered that oxalic acid was formed by fusing cellulose, sawdust, sugar, etc., with potassium hydroxide. This process was introduced into practical manufacture in 1856 by Dale.

Properties and Reactions.—Free oxalic acid crystallizes with two molecules of water in monoclinic prisms, which effloresce at 20° in dry air. On rapid heating, the hydrated acid melts at 101° and the anhydrous at 189° (Ber. **21**, 1901). It is soluble in 9 parts of water at ordinary temperatures, fairly easily in alcohol, but with difficulty in ether (C. 1897, I. 539). Anhydrous oxalic acid crystallizes from concentrated sulphuric and nitric acid (Ber. **27**, R. 80), and can be employed as a means of bringing about condensations on account of its dehydrating properties (Ber. **17**, 1078). When carefully heated to 150° the anhydrous acid sublimes undecomposed. Oxalic acid is poisonous.

(1) Rapidly heated it decomposes into formic acid and carbon dioxide, and also into CO_2, CO and water:

$$C_2H_2O_4 = CH_2O_2 + CO_2; \quad C_2H_2O_4 = CO_2 + CO + H_2O.$$

Reaction between oxalic acid and glycerol, see p. 282.

(2) An aqueous oxalic acid solution under the influence of light and air decomposes into CO_2, H_2O, and in the presence of sufficient oxygen, H_2O_2 (Ber. **27**, R. 496).

(3) Oxalates decompose into carbonate and hydrogen by fusion with alkalis or soda-lime:

$$C_2O_4K_2 + 2KOH = 2K_2CO_3 + H_2.$$

(4) Heated with concentrated sulphuric acid it yields carbon monoxide, dioxide and water.

(5) Nascent hydrogen converts it first into glyoxylic acid (p. 455) and then into glycollic acid (p. 414).

(6) Concentrated nitric acid slowly oxidizes oxalic acid to CO_2 and water. Potassium permanganate in acid solution rapidly oxidizes it, a reaction which is used in volumetric analysis.

Persulphates in acid solution and in presence of silver salts oxidize oxalic acid very energetically. This reaction constitutes a quantitative method for determining the active oxygen of persulphates (Ber. **38**, 3963).

A solution of mercuric chloride and ammonium oxalate rapidly decomposes, in the light and in absence of oxygen, into carbon dioxide and calomel (Ber. **38**, 2602).

(7) Anhydrous oxalic acid yields with phosphorus pentachloride, oxalyl chloride (p. 538). It has also been possible to replace 2Cl by O in certain organic dichlorides by using anhydrous oxalic acid (p. 318). $SbCl_5$ and oxalic acid yield the compound $(COOSbCl_4)_2$ (Ann. **239**, 285: **253**, 112: Ber. **35**, 1119).

Salts.—The *oxalates*, excepting those with the alkali metals, are almost insoluble in water.

Potassium oxalate, $C_2O_4K_2 + H_2O$. *Potassium hydrogen oxalate*, C_2O_4HK, dissolves with more difficulty than the neutral salt, and occurs in the juices of plants, such as *Oxalis* and *Rumex*. *Potassium quadrioxalate*, $C_2O_4KH{\cdot}C_2O_4H_2 + 2H_2O$.

Ammonium oxalate, $C_2O_4(NH_4)_2 + H_2O$, consists of shining, rhombic prisms, which occur in lævo- and dextro-hemihedral crystals (Ber. **18**, 1394: C. 1905, II. 885). *Calcium oxalate*, $C_2O_4Ca + H_2O$, is insoluble in acetic acid, and serves for the detection of calcium and of oxalic acid, both of which are determined quantitatively in this form. The *silver salt*, $C_2O_4Ag_2$, explodes when quickly heated.

Oxalic acid yields crystalline compounds with substances containing oxygen, such as cinnamic aldehyde, cineol, and dimethyl pyrone (Vol. II) (Ber. **35**, 1211).

Trimercuriacetic acid, $HOHg(Hg_2O)C{\cdot}COOH$, and *mercarbide*, $HOHg(Hg_2O)C{\cdot}C(Hg_2O)HgOH$ (*cf.* p. 144), are derivatives of oxalic acid. They are obtained when acetic acid or alcohol is heated with HgO in the presence of alkalis. They consist of white powders of basic character. Mercarbide is very stable towards reagents, but explodes violently when heated above 200° (Ber. **33**, 1328: **36**, 3707: **38**, 3654).

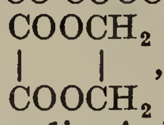
Esters.—The mono- and dialkyl esters of oxalic acid are formed simultaneously by heating anhydrous oxalic acid with alcohols. They can be separated by distillation under reduced pressure (Ann. **254**, 1).

Mono Alkyl Esters.—*Ethyl hydrogen oxalate*, $COOH{\cdot}COOEt$, b.p. 117°/15 mm., $D_{20} = 1{\cdot}2175$. n-*propyl ester*, $CO_2{\cdot}C_3H_7{\cdot}CO_2H$, b.p. 118°/13 mm. Preserved in sealed tubes, the alkyl hydrogen esters decompose into anhydrous oxalic acid and the neutral esters. Distilled at the ordinary temperature, they break down mainly into oxalic ester, CO_2, CO and H_2O, and in part to CO_2 and formic esters.

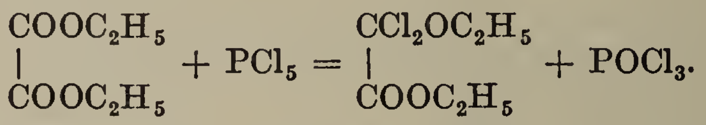
Dialkyl Esters.—The *methyl ester*, $C_2O_4(CH_3)_2$, is a crystalline solid, m.p. 54°, b.p. 153°. It can be used for the preparation of pure methyl alcohol, the crude alcohol being converted into the crystalline oxalate and the latter decomposed into oxalic acid and the pure aqueous alcohol.

Ethyl ester, b.p. 186°, is formed upon heating oxomalonic ester (Ber. **27**, 1304). See p. 483 for its conversion into carbonic ester. Oxalic ester, under the influence of sodium ethoxide, condenses with acetic ester to form oxalacetic ester, $CO_2C_2H_5{\cdot}CO{\cdot}CH_2{\cdot}CO_2C_2H_5$, and with acetone to acetone oxalic ester (comp. chelidonic acid). Zinc and alkyl iodides convert the oxalic ester into dialkylglycollic esters (p. 411).

Oxalic ester unites with hydroferrocyanic acid to form a well-crystallizing compound $(COOC_2H_5)_2 \cdot H_4Fe(CN)_6$ (Ber. **34**, 2692). With $SbCl_5$ ethyl oxalate forms $Cl_4SbC_2H_4OCO \cdot COOC_2H_3(SbCl_4)_2$ (Ber. **35**, 1120).

Ethylene ester,  $\begin{array}{l} COOCH_2 \\ | \quad\quad | \\ COOCH_2 \end{array}$, m.p. 143°, b.p. 197°/9 mm. (Ber. **27**, 2941).

Semi-ortho-oxalic Acid Derivatives.—*Dichloroxalic esters*: When PCl_5 acts on the neutral oxalic esters, one of the doubly-linked oxygen atoms is replaced by 2Cl atoms:



$$\begin{array}{l} COOC_2H_5 \\ | \\ COOC_2H_5 \end{array} + PCl_5 = \begin{array}{l} CCl_2OC_2H_5 \\ | \\ COOC_2H_5 \end{array} + POCl_3.$$

These products are called dichloroxalic esters (Ber. **28**, 61, note). When fractionated under greatly reduced pressure, they can be separated from unaltered oxalic ester. Distilled at the ordinary pressure, these esters decompose into alkyl chlorides and alkyl oxalic acid chlorides (see below).

Dichloroxalic dimethyl ester, $CCl_2(OCH_3) \cdot CO_2CH_3$, b.p. 72°/12 mm. $D_{22} = 1 \cdot 36$. *Dichloroxalic diethyl ester,* b.p. 85°/10 mm. *Dichloroxalic di-*n*-propyl ester,* b.p. 107°/10 mm.

Ethyl dichloroxalic chloride, $COCl \cdot CCl_2 \cdot OC_2H_5$, b.p. 140°, results from trichlorovinyl ethyl ether, $CCl_2 : CClOC_2H_5$, by absorption of oxygen (Ann. **308**, 324).

Semi-ortho-oxalic esters are produced by the interaction of dichloroxalic esters with sodium alcoholates in ether:

$$CO_2C_2H_5 \cdot CCl_2OC_2H_5 + 2C_2H_5ONa = CO_2C_2H_5 \cdot C(OC_2H_5)_3 + 2NaCl.$$

Tetramethyl oxalic ester, $C(OCH_3)_3 \cdot COOCH_3$, b.p. 76°/12 mm.; $D = 1 \cdot 1312$. *Tetraethyl oxalic ester,* b.p. 98°/12 mm. (Ann. **254**, 31).

The *anhydride* of oxalic acid is not known. In attempting to prepare it CO_2 and CO are produced. However, the chlorides of the alkyl oxalic acids, and oxalyl chloride, are known.

Chlorides of alkyl oxalic acids are obtained by the action of $POCl_3$ on potassium alkyl oxalates, and of $SOCl_2$ on alkyl hydrogen oxalates (Ber. **37**, 3678). They are most practically prepared by boiling dichloroxalic esters under the ordinary pressure until the evolution of alkyl chloride ceases (Ann. **254**, 26). They show the reactions of an acid chloride (p. 315). With benzene hydrocarbons and Al_2Cl_6 they yield phenyl glyoxylic esters and their homologues (Ber. **14**, 1689 : **29**, R. 511, 546). At 200° they break down into CO and chloroformic esters.

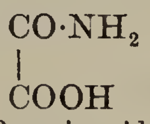
Methyl oxalic chloride, $COCl \cdot CO_2CH_3$, b.p. 119°; $D_{20} = 1 \cdot 3316$. *Ethyl oxalic chloride,* $COCl \cdot CO_2C_2H_5$, b.p. 135°; $D = 1 \cdot 2223$. n-*Propyl oxalic chloride,* b.p. 153°. iso*Butyl oxalic chloride,* b.p. 164°. *Amyl oxalic chloride,* b.p. 184°. These are liquids with a penetrating odour.

Oxalic mono-ethyl ester anhydride, $(C_2H_5OCO \cdot CO)_2O$, b.p. 135°/100 mm., is prepared by heating ethyl oxalic chloride and sodium acetate together, and fractionating the product of reaction (C. 1900, II. 174).

Oxalyl chloride, $COCl \cdot COCl$, m.p. − 12°, b.p. 64°, is obtained from anhydrous oxalic acid and phosphorus pentachloride. It readily breaks down into phosgene and carbon monoxide (Ber. **41**, 3563).

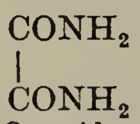
Amides of Oxalic Acid

Oxalic acid yields two amides: oxamic acid, corresponding with the mono-ethyl oxalic ester, and oxamide, corresponding with oxalic diethyl ester. Oximide can be included with these:



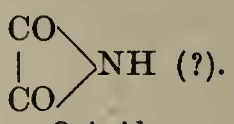
$\begin{array}{l} CO \cdot NH_2 \\ | \\ COOH \end{array}$

Oxamic acid.



$\begin{array}{l} CONH_2 \\ | \\ CONH_2 \end{array}$

Oxamide.

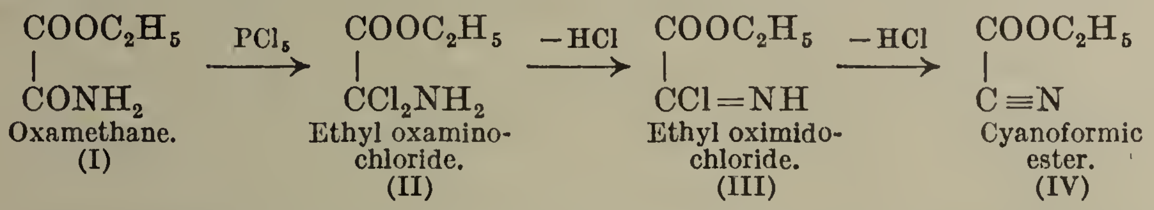


$\begin{array}{l} CO \\ | \\ CO \end{array} \!\!> NH$ (?).

Oximide.

Oxamic acid, $CONH_2 \cdot COOH_2$, m.p. 210° (decomp.). Its *ammonium salt* (*Balard,* 1842) is produced (1) by heating ammonium hydrogen oxalate; (2) from oxamide; and (3) by boiling oxamic acid esters with ammonia (Ber. **19**, 3229 : **22**, 1569). Hydrochloric acid precipitates oxamic acid from its ammonium salt as a difficultly soluble crystalline powder.

Its *esters* result from the action of alcoholic or dry ammonia on the esters of oxalic acid: *ethyl ester, oxamethane*, $CONH_2 \cdot COOC_2H_5$, m.p. 114° (*Boullay* and *Dumas*, 1828). Oxamethane yields with phosphorus pentachloride the dichloro derivative (II), which loses one molecule of HCl to form the imidochloride (III), and a further molecule of HCl to form ethyl cyanoformate (IV) (Wallach, Ann. **184**, 1):

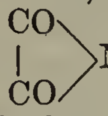


Oxamic trimethyl ortho-ester, $CONH_2 \cdot C(OCH_3)_3$, m.p. 115°, is formed on heating semi-ortho-oxalic methyl ester with anhydrous methyl alcoholic ammonia.

Methyloxamic acid, $CONH(CH_3) \cdot CO_2H$, m.p. 146°.

Ethyloxamic acid, $CONH(C_2H_5)CO_2H$, m.p. 120°.

Diethyloxamic acid, diethyloxamethane, $CON(C_2H_5)_2CO_2R$, b.p. 254°, is produced by the action of diethylamine on oxalic esters. It regenerates diethylamine on being distilled with potassium hydroxide. A method for separating the amines (p. 193) is based on this behaviour.

Oxalimide,  $\begin{matrix}CO\\ |\\ CO\end{matrix}\!\!>NH$ (?), is obtained from oxamic acid by the aid of PCl_5 or PCl_3O (Ber. **19**, 3229). The molecule is probably a double one.

Oxamide, $C_2O_2(NH_2)_2$, separates as a white, crystalline powder, when neutral oxalic ester is shaken with aqueous ammonia (1817, *Bauhof*). It is insoluble in water and alcohol. It is also formed on heating ammonium oxalate (1830, *Dumas*: 1834, *Liebig*); and when water and a trace of aldehyde act on cyanogen, C_2N_2; or by the direct union of hydrocyanic acid and hydrogen peroxide:

$$2HNC + H_2O_2 = C_2O_2N_2H_4.$$

Oxamide is partially sublimed when heated, the greater part, however, being decomposed. When heated to 200° with water, it is converted into ammonium oxalate. P_2O_5 converts it into cyanogen; heating with concentrated sulphuric acid, into ammonium sulphate, CO_2 and CO (Ber. **39**, 57).

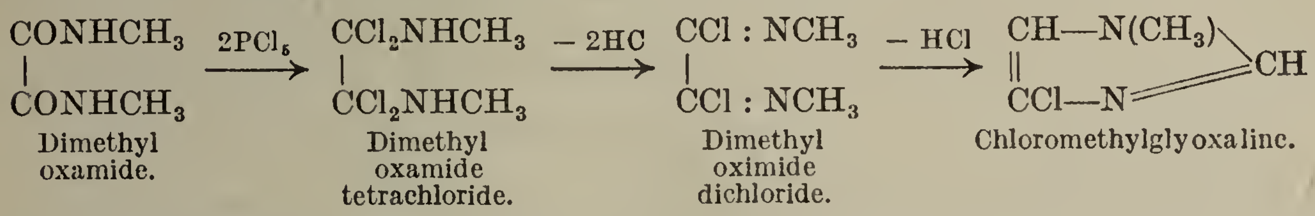
Alkyloxamides are produced by the action of the primary amines on the oxalyl esters.

sym.-*Dimethyloxamide*, $(CONHCH_3)_2$, m.p. 210°.

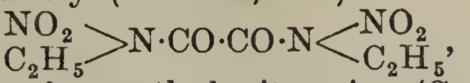
sym.-*Diethyloxamide*, $(CONC_2H_5)_2$, m.p. 179°.

Tetramethyloxamide, $[CON(CH_3)_2]_2$, m.p. 80°, is obtained from dimethylcarbamyl chloride by the action of sodium (Ber. **28**, R. 234).

PCl_5 converts these alkyloxamides into amide chlorides, which lose 3HCl and pass into glyoxaline derivatives (*Wallach*, Ann. **184**, 33: *Japp*, Ber. **15**, 2420): thus dimethyloxamide yields chloroxalomethyline (chloromethylglyoxaline) and diethyloxamide yields chloroxalethyline:



Oxamidoacetic acid, amidoxalylglycocoll, $NH_2CO \cdot CONH \cdot CH_2CO_2H$, m.p. 224–228° with decomposition, and *oxalyldiglycocoll, oxamidodiacetic acid*, $CO_2HCH_2 \cdot NHCOCONH \cdot CH_2CO_2H$, are formed from oxamethane and oxalic ester and glycocoll respectively (Ber. **30**, 580).

Diethyldinitro-oxamide,  $\begin{matrix}NO_2\\ C_2H_5\end{matrix}\!\!>N \cdot CO \cdot CO \cdot N<\!\!\begin{matrix}NO_2\\ C_2H_5\end{matrix}$, m.p. 35°, is decomposed by dilute sulphuric acid to form ethyl nitramine (C. 1898, I. 373).

Hydrazides and hydroxyamides of oxalic acid, *semi-oxamazide, oxaminic hydrazide*, $NH_2COCONH \cdot NH_2$, m.p. 220° (decomp.), is prepared from oxamethane and hydrazine. Similarly to semicarbazide, it gives condensation products with aldehydes and ketones (Ber. **30**, 585).

Oxamazide, $NH_2 \cdot CO \cdot CO \cdot N_3$, explodes by friction, or on heating to 115°.

Oxalic hydrazide, $NH_2 \cdot NHCOCO \cdot NHNH_2$, decomposes at about 235°, and turns brown. It is formed when hydrazine hydrate acts on oxalic ester. It unites with acetoacetic ester to form bis-acetoacetic ester oxalhydrazone, $(C_6H_{10}O_2) : NNHCOCONHN : (C_6H_{10}O_2)$ (Ber. **40**, 711).

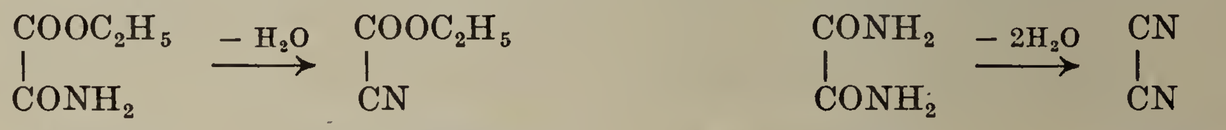
The reaction products of diazoacetic acid (p. 458) can be looked on as being cyclic hydrazine derivatives of oxalic acid; they yield hydrazine and oxalic acids when hydrolysed.

Hydroxyloxamide, $NH_2COCONH \cdot OH$, m.p. 159°, is formed from oxamethane and hydroxylamine.

Acetoxyloxamide, $NH_2COCONH \cdot OCOCH_3$, m.p. 173°, when heated with acetic anhydride to 110° is decomposed into cyanuric acid (p. 520) and acetic acid (Ann. **288**, 314 : *cf.* C. 1901, II. 210, 402). *Amidoxime oxalic acid*, $HOOC \cdot C(NOH)NH_2$ (Ann. **321**, 357).

Nitriles of Oxalic Acid

Two nitriles correspond with each dicarboxylic acid: a nitrilic acid, or semi-nitrile, and a dinitrile. The nitrilic acid of oxalic acid is cyanoformic acid, and it is only known in its esters. Cyanogen is the dinitrile of oxalic acid. The connection between these nitriles and oxalic acid is shown by their formation from the oxamic esters and oxamide through the elimination of water, and their conversion into oxalic acid by the absorption of water and the loss of ammonia:



$$\begin{array}{c} COOC_2H_5 \\ | \\ CONH_2 \end{array} \xrightarrow{-H_2O} \begin{array}{c} COOC_2H_5 \\ | \\ CN \end{array} \qquad \begin{array}{c} CONH_2 \\ | \\ CONH_2 \end{array} \xrightarrow{-2H_2O} \begin{array}{c} CN \\ | \\ CN \end{array}$$

Oxamethane. Cyanoformic ethyl ester. Oxamide. Cyanogen.

Cyanoformic esters, *cyanocarbonic esters*, *nitrilo-oxalic esters*, are produced during the distillation of oxamic esters with P_2O_5 or PCl (p. 325), as well as from cyanimidocarbonic ether. *Cyanoformic methyl ester*, $CN \cdot CO_2CH_3$, b.p. 100°. *Ethyl ester*, b.p. 115°. These are liquids with a penetrating odour. They are insoluble in water, which slowly decomposes them into CO_2, hydrocyanic acid, and alcohols. Zinc and hydrochloric acid convert them into glycocoll (p. 440). Concentrated hydrochloric acid breaks them down into oxalic acid, ammonium chloride, and alcohols. Bromine or gaseous HCl at 100° converts the ethyl ester into the polymeric cyanuric tricarboxylic esters (p. 522).

Cyanimidocarbonic acid ether, *oxalic nitrile imido ether*, $CN \cdot C(:NH)OC_2H_5$, b.p. 50°/30 mm., is prepared from cyanogen chloride or bromide and water, alcohol, and potassium cyanide; also from potassium cyanide, water, and ethyl hypochlorite (p. 169). Cyanimidocarbonic acid ether forms a yellow, sweet oil, possessing, at the same time, a pungent odour. Concentrated hydrochloric acid converts it into ammonium chloride and cyanocarbonic acid ester.

Chloroethyl imidoformyl cyanide, *oxalic nitrile ethyl imidochloride*, $CN \cdot C(:NC_2H_5)Cl$, b.p. 126°, is prepared from cyanogen chloride and ethyl *iso*cyanide (Ann. **287**, 302).

Cyanorthoformic ester, *triethoxyacetonitrile*, *ortho-oxalonitrilic ethyl ester*, $CN \cdot C(OC_2H_5)_3$, b.p. 160° (Ann. **229**, 178).

Trinitroacetonitrile, $CNC(NO_2)_3$, m.p. 41·5°, explodes at 220° (see fulminuric acid, p. 296).

Cyanogen, *oxalonitrile*, [ethane dinitrile], $CN \cdot CN$, is present in small quantity in the gases of the blast furnace. It was obtained in 1815 by Gay-Lussac by the ignition of mercuric cyanide. The change proceeds more readily by the addition of mercuric chloride:

$$Hg(CN)_2 = C_2N_2 + Hg. \qquad Hg(CN)_2 + HgCl_2 = C_2N_2 + Hg_2Cl_2.$$

Silver and gold cyanides behave similarly. Cyanogen is most readily prepared from potassium cyanide, by adding gradually a concentrated aqueous solution of 1 part KNC to 2 parts cupric sulphate in 4 parts of water, and then heating. At first a yellow precipitate of cupric cyanide, $Cu(CN)_2$, is produced, but immediately breaks up into cyanogen gas and cuprous cyanide, CuCN (Ber. **18**, R. 321):

$$2CuSO_4 + 4KNC = Cu_2(CN)_2 + (CN)_2 + 2K_2SO_4.$$

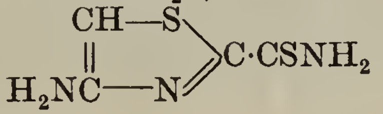
Its preparation by heating ammonium oxalate, and from oxamide and P_2O_5, is of theoretical interest.

Properties and Reactions.—Cyanogen is a colourless, peculiar-smelling, poisonous gas. It may be condensed to a mobile liquid which boils at $-21°$, and has $D = 0·866$, or by a pressure of five atmospheres at ordinary temperatures; at $-34°$ it forms a crystalline mass. It burns with a bluish, purple-mantled flame. Water dissolves 4 volumes and alcohol 23 volumes of the gas.

On standing, the solutions become dark and break down into ammonium oxalate and formate, hydrogen cyanide and urea, and at the same time a brown body, the so-called *azulmic acid*, $C_4H_5N_5O$, separates. With aqueous potassium hydroxide cyanogen yields potassium cyanide and cyanate. In these reactions the molecule breaks down, but if a slight quantity of aldehyde be present in the aqueous solution, only oxamide results. Oxalic acid is produced in the presence of mineral acids, $C_2N_2 + 4H_2O = C_2O_4H_2 + 2NH_3$. When heated with concentrated hydriodic acid it is converted into glycocoll (p. 440). Cyanogen unites with acetylacetone (p. 403), with sodium acetoacetic ester (p. 473), and with sodium malonic ester (p. 543).

Paracyanogen.—On heating mercuric cyanide there remains a dark substance, paracyanogen, a polymeric modification, $(C_2N_2)_n$. Strong ignition converts it again into cyanogen. It yields potassium cyanate with potassium hydroxide.

Thioamides of Oxalic Acid.—*Rubeanic acid, dithio-oxamide*, $CSNH_2·CSNH_2$, and *flaveanic acid, cyanothioformamide*, $CS·NH_2·CN$, m.p. 87–89° (decomp.), are formed when H_2S and cyanogen interact. They can be separated by means of chloroform, in which rubeanic acid is soluble with difficulty, and which deposits the flaveanic acid in the form of yellow, transparent, flat needles (Ann. **254**, 262). Rubeanic acid forms yellowish-red crystals. Primary bases cause the replacement of the amido-groups by alkyl amido-groups (Ann. **262**, 354). Aldehydes unite with rubeanic acid, with elimination of water (Ber. **24**, 1017).

Chrysean, $C_4H_5N_3S_2$, is prepared from KCN and H_2S, or thioformamide, $HCSNH_2$, and probably possesses the formula  $\begin{matrix}CH—S\diagdown \\ \| \quad\quad\; \rangle C·CSNH_2 \\ H_2NC—N\diagup\!\!\diagup\end{matrix}$ (Ber. **36**, 3546).

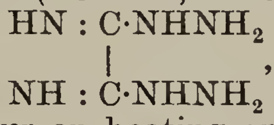
Thio-oxalic acid, HSCO·COSH (C. 1903, I. 816).

Diamido-oxalic ethers result from the action of ammonia on dichloroxalic esters, but have not yet been obtained in a pure condition. Aniline and dichloro-oxalic ether in cold ethereal solution, yield *dianilido-oxalic ether*, $CO_2C_2H_5C(NHC_6H_5)_2OC_2H_5$, a thick liquid, soluble in ether. At 0° hydrochloric acid precipitates from this ethereal solution the hydrochloride, $CO_2C_2H_5C(NHC_6H_5·HCl)_2OC_2H_5$. Mixed diamido-ethers can be obtained by allowing anhydrous ammonia gas to act on a cooled, ethereal solution of monophenylimido-oxalic acid dimethyl ether. In this way *amino-anilido-oxalic methyl ester*, $CO_2CH_3·C(NH_2)(NHC_6H_5)OCH_3$, is obtained, m.p. 215°.

Imido-oxalic ethers: *Mono-imido-oxalic ether*, $CO_2C_2H_5·C(:NH)OC_2H_5$, b.p. 73°/18 mm., results from the action of a calculated amount of $N/10$-hydrochloric acid on di-imido-oxalic acid (Ann. **288**, 289). *Phenylimido-oxalic methyl ether*, $CO_2CH_3·C(=N·C_6H_5)OCH_3$.

Di-imido-oxalic ether, $C_2H_5O·(NH)C—C(NH)·OC_2H_5$, m.p. 25°, b.p. 170°. Its hydrochloride is obtained on conducting HCl into an alcoholic solution of cyanogen (Ber. **11**, 1418) (*cf.* p. 540).

Oxalamidine, $NH_2(NH)C—C(NH)NH_2$, results from the action of alcoholic ammonia on the hydrochloride of oximido-ether (Ber. **16**, 1655).

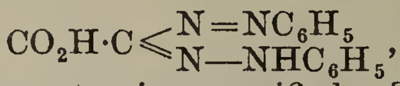
Carbohydrazidine, oxalodi-imide dihydrazide,  $\begin{matrix}HN:C·NHNH_2 \\ | \\ NH:C·NHNH_2\end{matrix}$, forms white, flat needles, which assume a reddish-brown colour on heating and do not melt at 250°. It results from the union of cyanogen with hydrazine. ***Dibenzal carbohydrazidine***, m.p. 218° (J. pr. Chem. [2] **50**, 253).

Oxalodihydroxamic acid, $[C(:NOH)OH]_2$, m.p. 165°, results from oxalic ester and hydroxylamine (Ber. **27**, 709, 1105).

Oxalodiamidoxime, $[C(:NOH)NH_2]_2$, m.p. 196°, with decomposition. It is formed when NH_2OH acts (1) on cyanogen (Ber. **22**, 1931), (2) on cyananiline (Ber. **24**, 801), (3) on hydrorubeanic acid (Ber. **22**, 2306) ; *dibenzoyl derivative*, m.p. 222° (Ber. **27**, R. 736).

Chloroximido-acetic ester, ethoxalo-oxime chloride, $CO_2C_2H_5\cdot C(:NOH)Cl$, m.p. 80°, is obtained from chloroacetoacetic ester by means of fuming nitric acid ; and when concentrated hydrochloric acid acts on nitrolacetic ester (Ber. **28**, 1217 : **39**, 784). Similarly, chloroacetoacetic ester and diazobenzene chloride yield *chlorophenylhydrazido-acetic ester, oxalic ester phenylhydrazido-chloride*, $CO_2R\cdot C(:NNHC_6H_5)Cl$ (C. 1902, II. 187).

Nitrolacetic ester, ethoxalonitrolic acid, $CO_2C_2H_5\cdot C(:NOH)\cdot NO_2$, m.p. 69°, is prepared from *iso*nitroso-acetoacetic ester and nitric acid of sp. gr. 1·2 (Ber. **28**, 1217).

Formazylcarboxylic acid,  $CO_2H\cdot C{<}\genfrac{}{}{0pt}{}{N{=}NC_6H_5}{N{-}NHC_6H_5}$, m.p. 162°, when rapidly heated, is produced when its ester is saponified. The ester results from the action of diazobenzene chloride (1) on the hydrazone of mesoxalic ester, (2) on sodium malonic ester, and (3) on acetoacetic ester. Just as oxalic acid breaks down into formic acid and CO_2, formazyl carboxylic acid decomposes into formazyl hydride (p. 289) and CO_2 (Ber. **25**, 3175, 3201).

The **ureides of oxalic acid**, parabanic acid, and oxaluric acid will be considered together with the derivatives of uric acid (*q.v.*).

The Malonic Acid Group

Malonic acid [propane diacid], $CH_2(CO_2H)_2$, occurs as its calcium salt in sugar-beets.

Formation.—(1) The acid was discovered in 1858 by *Dessaignes*, on oxidizing malic acid, $CO_2H\cdot CH(OH)\cdot CH_2CO_2H$, with potassium bichromate (hence the name, from *malum*, apple), and quercitol with potassium permanganate (Ber. **29**, 1764). It is also produced (2) in the oxidation of hydracrylic acid, and (3) of propylene and allylene by means of $KMnO_4$. (4) *Kolbe* and *Hugo Müller* obtained it almost simultaneously (1864) by the conversion of chloroacetic acid into cyanoacetic acid, the nitrile acid of malonic acid, and then saponifying the latter with potassium hydroxide. (5) By the decomposition of barbituric acid or malonylurea (*q.v.*). (6) Malonic ester and CO are formed in the distillation of oxaloacetic ester (*q.v.*) under the ordinary pressure (Ber. **27**, 795).

Preparation.—One hundred grams of chloroacetic acid, dissolved in 200 grams of water, are neutralized with sodium carbonate (110 grams), and to this 75 grams of pure, powdered potassium cyanide are added, and the whole carefully heated, after solution, upon a water-bath. The cyanide produced is hydrolysed either by concentrated hydrochloric acid or potassium hydroxide (Ber. **13**, 1358 : Ann. **204**, 225 : C. 1897, I. 282). To obtain the malonic ester directly, the cyanide solution is evaporated, the residue covered with absolute alcohol, and HCl gas led into it (Ann. **218**, 131), or it is treated with sulphuric acid and alcohol (C. 1897, I. 282).

Properties.—Malonic acid crystallizes in triclinic plates, m.p. 132°. It is easily soluble in water and alcohol. Above its melting point it decomposes into acetic acid and carbon dioxide. Halogens form substitution products, and by the breakdown of these, substituted acetic acids.

Salts.—*Barium salt,* $(C_3H_2O_4)Ba + 2H_2O$: *calcium salt,* $C_3H_2O_4Ca + 2H_2O$, dissolves with difficulty in cold water : *silver salt,* $C_3H_2O_4Ag_2$, is a white, crystalline compound.

Esters.—*Malonic mono-ethyl ester,* b.p. 147°/21 mm., is decomposed at higher temperatures into CO_2, acetic ester, acetic acid, and diethyl malonate : *potassium salt* is prepared from the neutral ester and one molecule of alcoholic potassium hydroxide. Electrolysis of this produces succinic ester (pp. 534, 548) (*cf.* C. 1900, II. 171 ; 1905, II. 30, where also are found ester-acids of alkylmalonic acids).

The *neutral malonic esters* are made by treating potassium cyanacetate or malonic acid with alcohols and hydrochloric acid. These compounds are of the first importance in the synthesis of the carboxylic acids, because of the replaceability of the hydrogen atoms of the CH_2-group by sodium.

History.—This property was first observed in 1874 by *van 't Hoff, Sr.* (Ber. **7**, 1383), and the possibility of obtaining the malonic acid homologues, by means of it, was indicated. The comprehensive, exhaustive experiments begun in 1879 by *Conrad* first demonstrated that malonic esters were almost as valuable as the acetoacetic esters in carrying out certain synthetic reactions (p. 470) (Ann. **204**, 121).

Methyl ester, $CH_2(CO_2CH_3)_2$, b.p. 181° ; *ethyl ester,* b.p. 198°, $D_{18} = 1{\cdot}068$. By the action of sodium ethoxide the compounds, $CHNa(CO_2C_2H_5)_2$ (p. 545) and $CNa_2(CO_2C_2H_5)_2$ (?), result (Ber. **17**, 2783 : **24**, 2889 : **32**, 1876 : **36**, 268). *Aluminium malonic ester,* $Al[CH(CO_2C_2H_5)]_3$, m.p. 95°, is formed by the action of aluminium amalgam on malonic ester (C. 1900, I. 12).

Reactions of Malonic Ester and its Metallic Derivatives. Iodine converts the sodium malonic esters into ethane- and ethylene-tetracarboxylic esters (*q.v.*). Sodium malonic ester, when electrolysed, yields ethanetetracarboxylic ester (Ber. **28**, R. 450). Alkyl halides convert the sodium malonic esters into esters of malonic acid homologues (Ber. **28**, 2616). These compounds are of importance in the synthesis of fatty acids (see p. 299).

When sodium acts on malonic ester at 70–90°, alcohol is given off, and there is formed the di-sodium compound of acetone tricarboxylic ester. This substance, acted on by sodium malonic ester at 145°, loses two further molecules of alcohol, whereby tri-sodium phloroglucinoltricarboxyylic ester is formed (Vol. II) (Ber. **32**, 1272) :

$$CO_2C_2H_5CHNa{\cdot}CNa(CO_2C_2H_5)_2 + CHNa(CO_2C_2H_5)_2 = C_6O_3Na_3(CO_2C_2H_5)_3 + 2C_2H_5OH.$$

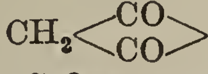
Malonic ester condenses with aldehydes under the influence of acetic anhydride, hydrochloric acid, sodium ethoxide, or small quantities of ammonia, diethylamine or piperidine. In the last case an intermediate product is formed —alkylidene bis-piperidine, which is converted by malonic ester into alkylidenebismalonic ester (Ber. **31**, 2585).

Free malonic acid also condenses with aldehydes and with some ketones, when heated with acetic acid, acetic anhydride, or pyridine ; water and CO_2 are split off and unsaturated carboxylic acids are formed (pp. 232, 338).

$\alpha\beta$-Olefinic aldehydes, $\alpha\beta$-olefinic ketones, and $\alpha\beta$-olefinecarboxylic esters unite with sodium malonic ester, a synthesis in which the $NaC(CO_2R)_2$ residue joins with the β-carbon atom, and the H-atom with the α-carbon atom. The aldehyde groups of the olefine aldehydes under these conditions unite also with two molecules of malonic ester (*cf.* Ann. **360**, 323).

Cyanogen combines with malonic ester in presence of a little sodium ethoxide to form cyanimino-*iso*succinic ester, $NC{\cdot}C(NH)CH(CO_2C_2H_5)_2$, and di-imino-oxalyl dimalonic ester, $(C_2H_5OCO)_2CHC(NH){\cdot}C(NH)CH(CO_2C_2H_5)_2$.

Diazobenzene chloride and malonic ester yield mesoxalic ester phenylhydrazone (*q.v.*).

Malonic anhydride,  $CH_2{<}^{CO}_{CO}{>}O$, is not known (see Carbon suboxide, below).

Carbon suboxide, C_3O_2, m.p. − 108°, b.p. + 7°, $D_0 = 1{\cdot}1137$, is formed by heating malonic ester or better malonic acid with phosphorus pentoxide (Diels, Ber. **41**, 82). It is also obtained by the action of the silent electric discharge on carbon monoxide (Nowak, 1910). It may be looked on as being a double malonic anhydride. In behaviour it resembles most nearly the ketens (pp. 269, 270), and is therefore to be looked on as carbon dicarbonyl or dioxoallene : $CO=C=CO$ (Z. angew. Chem. **39**, 661 : Ann. **439**, 76). Carbon suboxide polymerizes at ordinary temperatures to a dark-red solid mass. Water regenerates malonic acid ; ammonia and aniline produce malonamide and malonanilide. Hydrochloric acid forms malonyl chloride ; bromine produces dibromomalonyl bromide which re-forms carbon suboxide by the action of zinc in ether (Ber. **41**, 906) :

$$CH_2(COOH)_2 \underset{+\,2H_2O}{\overset{-\,2H_2O}{\rightleftarrows}} CO=C=CO \qquad CO=C=CO \underset{2Zn}{\overset{4Br}{\rightleftarrows}} BrCOCBr_2COBr.$$

Chlorides of Malonic Acid.—*Malonyl chloride monoethyl ester*, $CO_2C_2H_5\cdot CH_2COCl$, b.p. 69°/13 mm., is prepared from ethyl potassium malonate and PCl_5 ; or malonic ester and $SOCl_2$ (Ber. **25**, 1504 : C. 1905, II. 30 : also for homologous chloride esters).

Malonyl chloride, $CH_2(COCl)_2$, b.p. 58°/27 mm., is formed by the action of $SOCl_2$ on malonic acid, together with the monochloride, $HOCOCH_2COCl$, m.p. 65° (decomp.) (Ber. **41**, 2208).

Amides.—*Malonamic ester*, $CO_2C_2H_5\cdot CH_2CONH_2$, m.p. 50°, is formed when malonic ester imido-ether hydrochloride (see below) is heated ; also from malonyl chloride mono-ester and ammonia (Ber. **28**, 479 : C. 1905, II. 30).

Malonamide, $CH_2(CONH_2)_2$, m.p. 170°. *Malonic hydrazide*, $CH_2(CONH\cdot NH_2)_2$, m.p. 154°, reacts with aldehydes and ketones with loss of water (Ber. **39**, 3372 : **41**, 641).

Nitriles of Malonic Acid.—*Cyanoacetic acid, nitrilomalonic acid, malonic acid seminitrile*, $CN\cdot CH_2\cdot CO_2H$ (p. 533), m.p. 70° (Ber. **27**, R. 262), dissolves very readily in water, and at about 165° breaks down into CO_2 and acetonitrile (p. 324). *Cyanoacetic ethyl ester*, $CN\cdot CH_2\cdot CO_2C_2H_5$, b.p. 207° (for preparation, see C. 1905, I. 150), forms sodium derivatives like malonic ester (C. 1900, II. 38), by means of which the hydrogen of the CH_2-groups can be replaced by alkyls (Ber. **20**, R. 477) and acid radicals (Ber. **21**, R. 353). *Cyanacetamide*, $CN\cdot CH_2\cdot CONH_2$, is prepared from the ester and ammonia, m.p. 118°. *Cyanacetyl hydrazide*, $CNCH_2CO\cdot NHNH_2$, m.p. 114° (J. pr. Chem. [2] **51**, 186).

Cyanoacetic ester unites with alcohol and hydrochloric acid to form *malonic ester imido-ether hydrochloride*, $C_2H_5OCO\cdot CH_2C(:NH,HCl)OC_2H_5$, which, on digestion with alcohol, yields malonic semi-ortho-ester (*cf.* Ortho-esters, p. 330). The latter loses alcohol and passes into *diethoxyacrylic ester*, $(C_2H_5O)_2C=CH\cdot CO_2C_2H_5$, b.p. 128°/12 mm. This substance, when shaken with water, is converted into malonic ester ; bromine produces an oily dibromide, and with an increased quantity, dibromomalonic ester (Ber. **40**, 3358).

Malononitrile, methylene cyanide, $CH_2(CN)_2$, m.p. 30°, b.p. 218°, is obtained by distilling cyanacetamide with P_2O_5 (C. 1897, I. 32). It is soluble in water. Ammoniacal silver nitrate precipitates $CAg_2(CN_2)$ from the aqueous solution (Ber. **19**, R. 485). Hydrazine and malononitrile yield diamidopyrazole, $C_3N_2H_2(NH_2)_2$ (Ber. **27**, 690) (see also Cyanoform). *Malonic acid semi-amidoxime*, $NH_2(HON):C\cdot CH_2CO_2H$, m.p. 144° (Ber. **27**, R. 261 : Ann. **321**, 357). *Nitrilomalonimidoxime, cyanethenylamidoxime*, $CN\cdot CH_2C(:NOH)NH_2$, m.p. 124–127°. *Malondihydroxamic acid*, $CH_2[C(:NOH)OH]_2$, m.p. 154° (Ber. **27**, 803). *Malondiamidoxime*, $CH_2\cdot[C(:N\cdot OH)NH_2]_2$, m.p. 163–167° (Ber. **29**, 1168).

The **ureides of malonic acid** and cyanoacetic acid will be treated later in connection with uric acid (*q.v.*).

Halogen-substituted malonic acids are formed by the action of chlorine or sulphuryl chloride, bromine or iodine and iodic acid on malonic acid or its esters. Such malonic and alkylmalonic acids (see below) easily part with CO_2 and form α-halogen fatty acids, some of which are conveniently prepared in this way (Ber. **35**, 1374, 1813 : **39**, 351).

Chloromalonic acid, $CHCl(COOH)_2$; *ethyl ester*, b.p. 222°.

Bromomalonic acid, $CHBr(COOH)_2$, m.p. 113° (decomp.), *methyl ester*, b.p. 215–225°.

Dichloromalonic acid, $CCl_2(COOH)_2$; *ethyl ester*, b.p. 231–234° ; *amide*, m.p. 203°. **Dibromomalonic acid**, $CBr_2(COOH)_2$, m.p. 137° (Ann. **416**, 233) ; *dimethyl ester*, m.p. 64° ; *nitrile*, m.p. 65° (C. 1897, I. 32) ; *bromide*, b.p. 92°/13 mm. (see p. 543, Carbon suboxide). *Dibromomalonamide*, m.p. 200°. **Di-iodomalonic acid**, $CI_2(COOH)_2$, is prepared from malonic acid, iodine, and iodic acid in formic acid. It is extremely unstable; *methyl ester*, m.p. 80°, can be obtained from dibromomalonic ester and KI.

The mono- and di-halogen malonic acids serve as a connecting link between malonic acid and tartronic and mesoxalic acids. *Monobromo-* and *mono-iodocyano-acetic esters*, $CN{\cdot}CHXCO_2R$, are obtained from sodium cyanoacetic ester with bromine or iodine in the cold. At higher temperatures dicyanosuccinic ester and tricyano-trimethylene tricarboxylic esters are formed (C. 1900, II. 38, 1202).

Nitromalonic Acid, $NO_2{\cdot}CH(COOH)_2$. The *ethyl ester*, b.p. 127°/10 mm., and *amide*, are obtained by the action of nitric acid on malonic ester or malonamide (C. 1901, I. 1196: 1902, I. 1198: 1904, II. 1109). *Dimethylamide*, $NO_2{\cdot}CH(CO{\cdot}NHMe)_2$, m.p. 156° (Ber. **28**, R. 912). *Nitromethylmalonic ester*, $NO_2{\cdot}CMe(COOEt)_2$, is obtained by the action of methyl iodide on the ammonium salt of nitromalonic ester. The higher alkylmalonic esters are obtained by the nitration of the alkylmalonic esters. These compounds are decomposed into nitro-fatty acid esters by the action of sodium ethoxide (C. 1904, II. 1600). Fulminuric acid, $CN{\cdot}CH(NO_2){\cdot}CONH_2$ (p. 296), can be regarded as a derivative of nitromalonic acid.

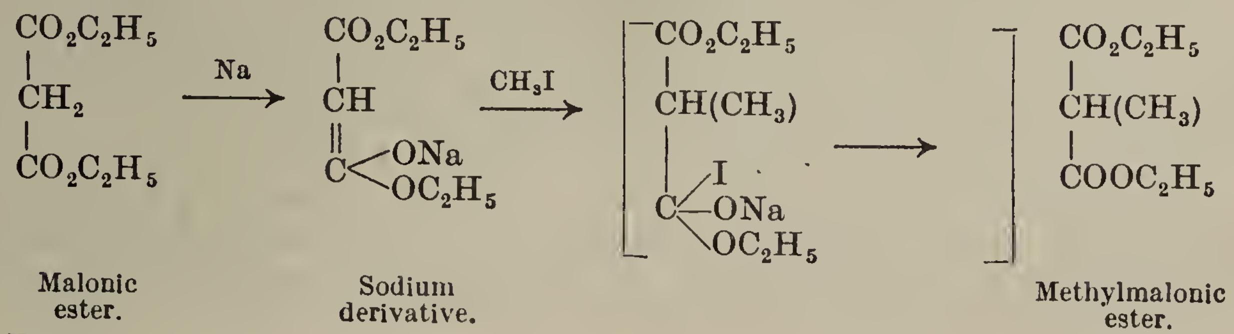
Aminomalonic acid, $NH_2{\cdot}CH(COOH)_2$, shining prisms, m.p. 109° (decomp.), is formed by the reduction of *iso*nitrosomalonic acid (p. 618), by the action of ammonia on chloromalonic acid (Ber. **35**, 2550) and by the alkaline hydrolysis of uramil (p. 632, Ann. **333**, 77). The aqueous solution decomposes into glycine and carbon dioxide when warmed. The esters are obtained from the acid or by reduction of the *iso*nitrosomalonic esters. *Methyl ester hydrochloride*, m.p. 159° (decomp.). *Ethyl ester hydrochloride*, m.p. 162° (decomp.). The *amide*, $NH_2{\cdot}CH(CONH_2)_2$, m.p. 192° (decomp.), is obtained from the esters and ammonia (Ber. **39**, 514) or, together with iminodimalonamide, $NH[CH(CONH_2)_2]_2$, by the action of alcoholic ammonia on chloromalonic ester at 130° (Ber. **15**, 607). *Aminomalononitrile*, $NH_2{\cdot}CH(CN)_2$, m.p. 184°, is a polymer of hydrocyanic acid, (p. 284: Ber. **35**, 1083).

Anilinomalonic acid, $C_6H_5NH{\cdot}CH(COOH)_2$, m.p. 121° (C. 1897, II. 568: (1898, I. 829) (for the condensation of the esters to indoxylic esters, see Indigo, Vol. III).

Phthalimidomalonic ester, $C_6H_4(CO)_2N{\cdot}CH{\cdot}(COOEt)_2$, m.p. 74°, is obtained from potassium phthalimide and bromomalonic ester (C. 1903, II. 33).

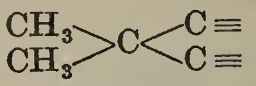
Monothio-bis-malonic ester, $S[CH(CO_2R)_2]_2$, *dithio-bis-malonic ester*, $S_2[CH(CO_2R)_2]_2$, and *tri-thio-bis-malonic ester*, $S_3[CH(CO_2R)_2]_2$, are formed from malonic ester and S_2Cl_2 (Ber. **36**, 3721).

Alkylmalonic Acids.—The general methods suitable for the preparation of alkylmalonic acids are (1) reaction 5*a* (p. 533), conversion of α-halogen fatty acids into α-cyano-fatty acids—the half nitriles of the malonic acid homologues; and (2) reaction 6 (p. 534), the replacement of the hydrogen atoms of the CH_2 group in the malonic esters by alkyls. First, with the aid of sodium ethoxide, or sodium in ether (J. pr. Chem. [2] **72**, 537), monosodium malonic esters are made, which alkyl iodides convert into mono-alkylmalonic esters. These are further able to yield monosodium alkylmalonic esters, which alkyl halides change to dialkylmalonic esters—*e.g.*:



Alkylmalonic esters are also formed when alkyl oxaloacetic esters lose CO (Ber. **31**, 551).

Some of these dialkylmalonic acids are formed when complex carbon derivatives are oxidized—*e.g.* dimethylmalonic acid results from the oxidation of *unsym.*-dimethylsuccinic acid, mesitonic acid, camphor, etc. The production of dimethylmalonic acid in this manner proves the presence, in these bodies, of the grouping—



$$\begin{matrix} CH_3 \\ CH_3 \end{matrix} \!>\! C \!<\! \begin{matrix} C\equiv \\ C\equiv \end{matrix}$$

All mono- and dialkyl-malonic acids, when exposed to heat, lose CO_2 and pass into mono- (Ber. **27**, 1177) and dialkyl-acetic acids (p. 299).

See Z. physik. Chem. **8**, 452, for the affinities of the alkylmalonic acids. Consult Ber. **29**, 1864; J. pr. Chem. [2] **72**, 537, upon the velocity of hydrolysis of the alkylmalonic esters.

*iso***Succinic acid**, *methylmalonic acid*, *ethylidene succinic acid* [methyl-propane di-acid], $CH_3CH(CO_2H)_2$, m.p. 130° (decomp.), is isomeric with ordinary succinic acid (p. 547), and is obtained (1) from α-chloro- and α-bromo-propionic acids through the cyanide (Ber. **13**, 209), and (2) from sodium malonic ester and methyl iodide (Ann. **347**, 93).

When ethylidene bromide, $CH_3{\cdot}CHBr_2$, is heated with potassium cyanide and alkalis, the expected methylmalonic acid is not formed, but by molecular rearrangement, ordinary succinic acid results.

The acid is more soluble than ordinary succinic acid in water. If heated above 130°, it breaks up into carbon dioxide and propionic acid (p. 303); *ethyl ester*, b.p. 196°; *methyl ester*, b.p. 179°; *diamide*, m.p. 216°.

For the rules of formation of the *diamides* of homologous alkyl and di-alkylmalonic acids, see Ber. **39**, 1596: C. 1905, II. 725: 1906, I. 1235, etc.

α-Cyanopropionic ester, $CH_3CH(CN)CO_2C_2H_5$, b.p. 197–198°.

*Bromo*iso*succinic acid*, $CH_3CBr(CO_2H)_2$, m.p. 118–119° (Ber. **23**, R. 114); *methyl ester*, b.p. 115–118°/25 mm. (Ber. **26**, 2356).

Aminomethylmalonic acid, $NH_2{\cdot}CMe(COOH)_2$, is obtained from pyruvic acid by the action of hydrogen cyanide and alcoholic ammonia (Ber. **20**, R. 507).

Ethylmalonic acid, $C_2H_5{\cdot}CH(CO_2H)_2$, m.p. 111·5°. *Ethyl ester*, b.p. 200°; *amide*, m.p. 216°; *ethylbromomalonic ester*, b.p. 125° (Ber. **26**, 2357).

Dimethylmalonic acid, $(CH_3)_2C(CO_2H)_2$, m.p. 185° (decomp.) (Ann. **247**, 105); *ethyl ester*, b.p. 195°; *amide*, m.p. 261°; *nitrile*, m.p. 32°, b.p. 64°/22 mm.; *dichloride*, m.p. 165°. The latter, with aqueous pyridine, yields a polymeric anhydride, $[(CH_3)_2C(CO)_2O]_x$ (Ann. **359**, 169), which can also be formed by heating the *monochloride*, $HOCOC(CH_3)_2COCl$, m.p. 65° (decomp.), and also by prolonged heating yields dimethylketen (p. 271) (Ber. **41**, 2212).

In the case of the subjoined alkylmalonic acids, the boiling points of the ethyl esters (enclosed in parentheses) are given, together with the melting points of the acids.

Propylmalonic acid, $CH_3CH_2CHCH(CO_2H)_2$, m.p. 96° (219–222°).

iso*Propylmalonic acid*, $(CH_3)_2CH{\cdot}CH(CO_2H)_2$, m.p. 87° (213–214°).

Methylethylmalonic acid, $CH_3(C_2H_5)C(CO_2H)_2$, m.p. 118° (207–208°).

n-*Butylmalonic acid*, $CH_3(CH_2)_3{\cdot}CH(CO_2H)_2$, m.p. 101·5°. iso*Butylmalonic acid*, m.p. 107° (225°). sec.-*Butylmalonic acid*, $CH_3(C_2H_5)CH{\cdot}CH(CO_2H)_2$, m.p. 76° (234°). *Methylpropylmalonic acid*, $CH_3(CH_3{\cdot}CH_2CH_2)C(CO_2H)_2$, m.p. 107° (220–223°). *Methyl*iso*propylmalonic acid*, m.p. 124° (221°).

Diethylmalonic acid, m.p. 121° (Ann. **292**, 134); *dimethyl ester*, b.p. 205°; *chloride*, b.p. 197°, yields a polymeric anhydride, $[(C_2H_5)_2C(CO)_2O]_{12}$, when treated with pyridine and soda solution. Boiling in benzene partially de-polymerizes it, whilst when heated alone it is decomposed into diethyl keten (p. 271) and CO_2 (Ann. **359**, 159: Ber. **41**, 2216); *amide*, m.p. 224° (Ber. **35**, 854: Ann. **359**, 174: C. 1906, I. 1237). *Nitrile*, m.p. 44°, b.p. 92°/24 mm. *Veronal* is a ureide of this acid (see Barbituric acid).

n-*Amylmalonic acid*, $CH_3[CH_2]_4CH(CO_2H)_2$, m.p. 82°. *Dipropylmalonic acid*, $(CH_3CH_2CH_2)_2C(CO_2H)_2$, m.p. 158°. *Cetylmalonic acid*, $CH_3[CH_2]_{15}CH(CO_2H)_2$, m.p. 122° (Ann. **204**, 130: **206**, 357: Ber. **24**, 2781).

For *alkyl* and *di-alkyl cyanoacetic esters* and *amides*, see also Ann. **340**, 310.

The Succinic Acid Group

Succinic acid and its alkyl derivatives, as mentioned in the introduction, are characterized by the fact that when heated they break down into anhydrides and water. The anhydride formation takes place more readily in the alkylsuccinic acids, the more hydrogen atoms of the ethylene residue of the succinic acid are replaced by alkyl radicals.

The alkylsuccinic acids form anhydrides more readily with acetyl chloride, and are more volatile in aqueous vapour than their isomeric alkylglutaric acids (Ann. **285**, 212). The *sym.*-dialkylsuccinic acids show remarkable isomeric phenomena, which will be more fully discussed under the symmetrical dimethylsuccinic acids (p. 547).

The following serve to characterize a succinic acid: (1) the anhydride; (2) the anilic acid, which is formed in the chloroform, ethereal, or benzene solution of the anhydride by the action of aniline; (3) the anil, produced by heating the anilic acid, or by the action of phosphorus pentachloride or acetyl chloride on it (Ann. **261**, 145: **285**, 226: **309**, 316).

The anhydrides of the succinic acids unite with alcohols to form acid esters, which are also formed by partial esterification of the acids, and by partial hydrolysis of the neutral esters. In the case of the unsymmetrically substituted succinic acids, the first two methods usually yield identical products, the third method the isomeric ester (C. 1904, I. 1484: Ann. **354**, 117).

Succinic acid, $CO_2H \cdot CH_2CH_2 \cdot CO_2H$, is isomeric with methylmalonic acid, or *iso*succinic acid (p. 546). It occurs in amber, in some varieties of lignite, in resins, in turpentine oils, and in animal fluids. It is formed in the oxidation of fats with nitric acid, in the fermentation of calcium malate or ammonium tartrate (Ann. **14**, 214), and in the alcoholic fermentation of sugar (p. 141).

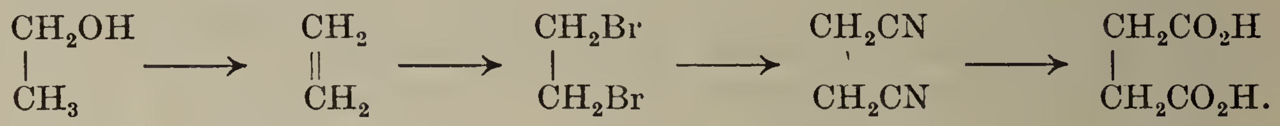
According to the general methods of formation (p. 533) succinic acid is produced (1) by the oxidation of γ-butyrolactone and of succinic dialdehyde.

(2) By the reduction of fumaric and maleic acids with nascent hydrogen.

(3) By reducing (*a*) malic acid (hydroxysuccinic acid) and tartaric acid (dihydroxysuccinic acid) with hydriodic acid, or by the fermentation of these bodies; (*b*) the action of sodium amalgam on halogen succinic acids.

(4) It is obtained in small quantities by the action of finely divided silver on bromoacetic acid.

(5*a*) By converting β-iodopropionic acid (p. 335) into the cyanide and decomposing the latter with alkalis or acids. (5*b*) *M. Simpson*, in 1861, was the first to prepare it synthetically from ethylene, by converting the latter into the cyanide. Succinic acid is formed by boiling its dinitrile with potassium hydroxide or mineral acids:



$$\begin{matrix}CH_2OH\\|\\CH_3\end{matrix}\longrightarrow\begin{matrix}CH_2\\\|\\CH_2\end{matrix}\longrightarrow\begin{matrix}CH_2Br\\|\\CH_2Br\end{matrix}\longrightarrow\begin{matrix}CH_2CN\\|\\CH_2CN\end{matrix}\longrightarrow\begin{matrix}CH_2CO_2H\\|\\CH_2CO_2H.\end{matrix}$$

Ethylidene chloride and potassium cyanide also yield ethylene cyanide (p. 554).

(6) By the electrolysis of potassium ethyl malonate (p. 543) ethyl succinate is produced.

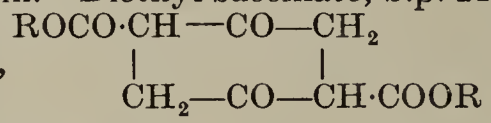
(7) By the decomposition of acetosuccinic esters, (8) of ethane tricarboxylic acid, (9) of *sym.*-ethane tetracarboxylic acid.

Properties.—Succinic acid crystallizes in monoclinic prisms or plates, and has a faintly acid, disagreeable taste. It melts at 185° and boils at 235° with decomposition into the anhydride and water. At the ordinary temperature it dissolves in 20 parts of water.

Uranium salts decompose aqueous succinic acid in sunlight into propionic acid and CO_2. The electric current decomposes the potassium salt into ethylene, carbon dioxide, and potassium (p. 103).

Paraconic acids (γ-lactone carboxylic acids) are formed when sodium succinate is heated with aldehydes and acetic anhydride (*Fittig*, Ann. **255**, 1). When succinic acid, zinc chloride, sodium acetate, and acetic anhydride are heated to 200°, small quantities of 2 : 5-dimethyl-3-acetylfuran (Ber. **27**, R. 405) are produced. When calcium succinate is distilled, 1 : 4-*cyclo*hexanedione (Vol. II) is produced in small quantities (Ber. **28**, 738).

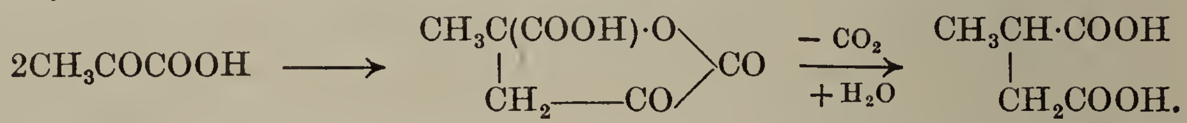
Succinates: *calcium salt*, $C_4H_4O_4Ca + 3H_2O$, separates from a cold solution, but when it is deposited from a hot liquid it contains only $1H_2O$. When ammonium succinate is added to a solution containing a ferric salt, all the iron is precipitated as reddish-brown *basic ferric succinate* (separation of iron from aluminium).

Esters.—*Potassium ethyl succinate* when electrolysed yields adipic ester (p. 561). *Monomethyl succinate*, m.p. 58°, is prepared from the anhydride and alcohol (C. 1904, I. 1484). *Dimethyl succinate*, $CO_2CH_3 \cdot CH_2 \cdot CH_2CO_2CH_3$, m.p. 19°, b.p. 80°/10 mm. Diethyl succinate, b.p. 216°. Sodium converts it into succinyl succinic ester,  (Vol. II). Ethylene succinate (Ann. **280**, 177).

Succinyl chloride, see p. 551. *Succinamide* and *succinimide*, see p. 552.

Mono-alkyl Succinic Acids

Pyrotartaric acid, *methylsuccinic acid*, $COOH \cdot CH(CH_3) \cdot CH_2 \cdot COOH$, m.p. 112°, was first obtained (1) by the dry distillation of tartaric acid. It is produced (2) from pyroracemic acid or its condensation product, keto-valerolactone carboxylic acid, when heated with hydrochloric acid (Ann. **317**, 22):



The remaining methods of formation correspond with those for the production of succinic acid; (3) by the reduction of ita-, citra-, and mesa-conic acids (p. 571); (4) from β-bromobutyric acid and propylene bromide by means of potassium cyanide; (5) from α- and β-methyl acetosuccinic esters; and (6) from α- and β-methyl ethane tricarboxylic acids.

The acid dissolves readily in water, alcohol, and ether. When quickly heated above 200° it decomposes into water and the anhydride. If, however, it be exposed for some time to a temperature of 200–210°, it splits into CO_2 and butyric acid. It undergoes the same decomposition when in aqueous solution, if acted on by sunlight in presence of uranium salts (Ber. **24**, R. 310).

Resolution into its optically active components is effected by strychnine (Ber. **29**, 1254). *Dextro-rotatory* pyrotartaric acid is also formed when menthone is oxidized.

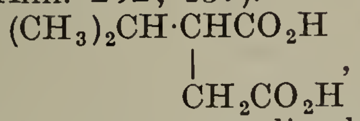
Potassium salt, $C_5H_6O_4K_2$; *calcium salt*, $C_5H_6P_4Ca + 2H_2O$, dissolves with difficulty in water.

Methyl ester, b.p. 153°/20 mm.; *ethyl ester*, b.p. 160°/23 mm.; *dimethyl ester*, b.p. 197°; *diethyl ester*, b.p. 218° (Ber. **26**, 337: C. 1900, I. 169: 1904, I. 1484).

Ethylsuccinic acid, m.p. 98°.

n-**Propylsuccinic acid** (Ann. **292**, 137).

*iso***Propylsuccinic acid**,



$$\begin{matrix}(CH_3)_2CH{\cdot}CHCO_2H\\ |\\ CH_2CO_2H\end{matrix}$$

, m.p. 115°, was first prepared by fusing camphoric acid and tanacetogen dicarboxylic acid (Ber. **25**, 3350) with potassium hydroxide. It may be synthetically obtained from acetoacetic or malonic esters (Ann. **292**, 137: **298**, 150), as well as from the products of the action of potassium cyanide on *iso*caprolactone at 280° (C. 1897, I. 408).

*iso***Butylsuccinic acid**, m.p. 107° (Ann. **304**, 270).

Symmetrical Dialkylsuccinic acids

Symmetrical dimethylsuccinic acid exists, like the other symmetrical disubstituted succinic acids—*e.g.* dibromosuccinic acid (p. 556), diethyl-, methylethyl-, di-*iso*propyl-, and diphenyl-succinic acids—in two different forms, having the same structural formulæ.

Dihydroxysuccinic acid or tartaric acid occurs in two active and two inactive forms (one can be resolved and the other cannot), which are satisfactorily explained by van 't Hoff's theory of asymmetric carbon atoms (p. 37). The pairs of isomeric dialkylsuccinic acids, also containing asymmetric carbon atoms, manifest certain analogies with paratartaric acid (racemic acid), and anti- or meso-tartaric acid. Hence it is assumed that their isomerism is due to the same cause. The higher melting, more difficultly soluble modification is called the *para*-form, whilst the *meso*- or *anti*-form is more readily soluble, and melts lower (*Bischoff*, Ber. **20**, 2990: **21**, 2106). Bischoff has set forth a theory of *dynamical isomerism* (Ber. **24**, 1074, 1085) in which he presents views in regard to the equilibrium positions of the atoms and radicals, joined to the two asymmetric carbon atoms, in the symmetrical dialkylsuccinic acids. Dimethylsuccinic acid has been resolved: see below.

Isomeric pairs of the dialkylsuccinic acids are formed (according to method 2, p. 533) by the reduction of dialkylmaleic anhydrides, such as pyrocinchonic anhydride (p. 574), by means of HI or sodium amalgam (Ber. **20**, 2737: **23**, 644); from α-monohalogen fatty acids by finely divided silver (method of formation 4) (Ber. **22**, 60); from α-monohalogen fatty acids by the action of potassium cyanide (Ber. **21**, 3160); from aceto-dialkyl-succinic esters by elimination of the acetyl group (method 8); from *sym.*-dialkylethanepolycarboxylic acids by heating them with hydrochloric acid (method 9) (*cf.* p. 534).

In all these reactions both dialkylsuccinic acids are formed together, and may be separated by crystallization from water.

sym.-**Dimethylsuccinic acids**, $CO_2H{\cdot}CH(CH_3){\cdot}CH(CH_3)CO_2H$.

The *para*-acid, m.p. 192–194°, is soluble in 96 parts of water at 14°. It forms needles and prisms, which lose some water upon melting. If the acid be heated for some time to 180–200°, it yields a mixture of the *anhydrides* of the *para*- and *anti*-acids, $C_6H_8O_3$, m.p. 38° and 87°. With water each reverts to its corresponding acid. When acetyl chloride acts on the *para*-acid, its *anhydride*, m.p. 38°, is the only product. This crystallizes from ether in rhombic plates, and unites with water to form the pure *para*-acid (Ber. **20**, 2741: **21**, 3171: **22**, 389: **23**, 641: **29**, R. 420).

If the *para*-acid be heated to 130° with bromine, it yields pyrocinchonic anhydride, $C_6H_6O_3$ (p. 574). Both acids, when digested with bromine and phosphorus, yield the same bromodimethylsuccinic acid, $C_6H_9BrO_4$, m.p. 91°. Zinc and hydrochloric acid change it to the *anti*-acid (Ber. **22**, 66). The *ethyl ester* of the *para*-acid (from the silver salt), b.p. 219°; *methyl ester*, b.p. 199°.

The *meso*- or *anti*-acid, m.p. 120–123° (after repeated crystallizations from water) dissolves in 33 parts of water at 14°. It crystallizes in shining prisms. It yields its *anhydride*, $C_6H_8O_3$, m.p. 87°, when heated to 200°. This regenerates the acid with water. If the *anti*-acid be heated with hydrochloric acid to 190°, it yields the *para*-acid. The *methyl ester*, b.p. 200° ; *ethyl ester*, b.p. 222°. When the *anti*-acid is esterified with HCl, it yields a mixture of the esters of the *anti*- and *para*-acid (Ber. **22**, 389, 646 : **23**, 639). The ethyl ester is also obtained when α-iodopropionic ester is shaken with mercury in sunlight (C. 1902, I. 408).

anti-s-Dimethylsuccinic acid has been resolved ($[\alpha]_D \pm 8°$: m.p. 135°) by means of the compound with a cobaltammine (*Werner*, Ber. **46**, 3229).

The *monomethyl ester* of the *para*-acid, m.p. 38°, and of the *anti*-acid, m.p. 49°, are obtained by the action of methyl alcohol on the anhydrides (C. 1904, I. 1484).

sym.-**Methylethylsuccinic acids,** $CO_2H{\cdot}CH(CH_3){\cdot}CH(C_2H_5)CO_2H$. The *para*-acid, m.p. 179° ; *anti*- or *meso*-acid, m.p. 101° (Ann. **298**, 147).

sym.-**Methyl*iso*propylsuccinic acids.** The *para*-acid, m.p. 174° ; *meso*-acid, m.p. 125° (Ber. **29**, R. 422).

sym.-**Diethylsuccinic acids.**—The *para*-acid, m.p. 189–192° ; *anti*-acid, m.p. 129° (Ber. **20**, R. 416 : **21**, 2085, 2105 : **22**, 67 : **23**, 650).

The para- and meso-forms of the sym.-*di*-n.-*propylsuccinic acid*, *di*-iso*propylsuccinic acid*, and *propyl*iso*propylsuccinic acid*, are prepared by the introduction of propyl or *iso*propyl groups into propyl- or *iso*propylcyanosuccinic ester followed by hydrolysis and decomposition of the condensation products. Di-*iso*-propylsuccinic acid also results from bromo*iso*valeric ester and silver (Ann. **292**, 162 : C. 1900, I. 846, 1205). Other *sym.*-dialkylsuccinic acids, see C. 1901, I. 167.

s-**Diphenylsuccinic acid**, two forms, m.p. 183° (+ H_2O), (222° anhyd.) and 229°. Both yield with concentrated sulphuric acid at 130° diphenylsuccindandione (Ber. **14**, 1802 : **45**, 3071).

Unsymmetrical Dialkylsuccinic Acids

asym.-**Dimethylsuccinic acid,** $CO_2H{\cdot}CH_2{\cdot}C(CH_3)_2{\cdot}CO_2H$, m.p. 140°, is synthesized from α-dimethylethanetricarboxylic ester by the action of boiling sulphuric acid. The ester is the reaction product of bromo*iso*butyric ester and sodium malonic ester (C. 1898, I. 885). It can also be obtained from dimethyl cyanoethanedicarboxylic ester, the product of reaction of sodium cyanoacetic acid and α-bromo*iso*butyric ester ; from the acid nitrile, the product of the interaction of potassium cyanide and β-chloro*iso*valeric acid (C. 1899, I. 182) ; also, from its nitrile (p. 554). The imide (p. 553) is obtained by oxidation of mesitylic acid. Esterification of *as*-dimethylsuccinic acid proceeds by first attacking the carboxyl group attached to the CH_2-group, producing the *α-mono-ethyl ester*, $CO_2H{\cdot}C(CH_3)_2{\cdot}CH_2CO_2C_2H_5$, m.p. 70°, b.p. 150°/14 mm. This substance can also be obtained by the action of alcohol on dimethylsuccinic anhydride. Partial hydrolysis of the *diethyl ester*, b.p. 215°, produces the liquid isomer *β-mono-ethyl ester* (Private communication of Anschütz and Güttes). *Monomethyl esters*, m.p. 42° and 51° (C. 1904, I. 1485).

as-**Methylethylsuccinic acid** (Ann. 292, 138, 153).

as-**Diethylsuccinic acid,** m.p. 86°.

Trimethylsuccinic acid, $CO_2H{\cdot}\overset{*}{C}H(CH_3)—C(CH_3)_2{\cdot}CO_2H$, m.p. 151° (Ann. **292**, 142), results on hydrolysing the tricarboxylic ester (Ber. **24**, 1923) produced in the action of bromo*iso*butyric ester on sodium methylmalonic ester, or sodium α-cyanopropionic ester, as well as in the oxidation of camphoric acid (Ber. **26**, 2337) ; and by fusing camphoronic acid with potassium hydroxide (Vol. II : Ann. **302**, 51). The formation of trimethylsuccinic anhydride from camphoronic acid by distillation is rather important in the recognition of the constitution of camphor (Ber. **26**, 3047). Trimethylsuccinic acid is resolved into its *optically active components* by means of the quinine salts (C. 1901, I. 513).

Tetramethylsuccinic acid, $CO_2H{\cdot}C(CH_3)_2{\cdot}C(CH_3)_2CO_2H$, m.p. 190–192°, with loss of water, is formed, together with trimethylglutaric acid (p. 558), when α-bromo*iso*butyric acid (or its ethyl ester) is heated with silver (Ber. **23**, 297 : **26**, 1458) ; also by electro-synthesis from potassium dimethylmalonic ester, and from azobutyronitrile (p. 452) (Ann. **292**, 220) ; *monomethyl ester*, m.p. 63°.

Tetraethylsuccinic acid, m.p. 149°, with conversion into anhydride, and **tetrapropylsuccinic acid,** m.p. 137°, are obtained by electrolysis of the respective dialkyl malonic mono-esters (C. 1905, II. 670 : 1906, II. 500).

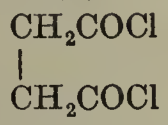
These tetraalkyl succinic acids pass very readily into their anhydrides.

Acid Chlorides of the Succinic Acid Group

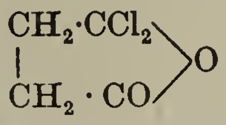
Of the possible chlorides, the *monochloride*, $Cl{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$, is only known in the form of its *ethyl ester*, b.p. 144°/90 mm., which results from the action of $POCl_3$ (Ber. **25**, 2748) on sodium succinic ethyl ester.

Succinyl chloride, m.p. 16°, b.p. 103°/25 mm., results from the action of PCl_5 on succinic acid.

Two formulæ have been suggested for this substance, a symmetrical (1), and an unsymmetrical one (2):

(1)


$$\begin{array}{l} CH_2COCl \\ | \\ CH_2COCl \end{array}$$

(2)


$$\left.\begin{array}{l} CH_2{\cdot}CCl_2 \\ | \\ CH_2 \cdot CO \end{array}\right\rangle O$$

This latter view would make succinyl chloride a dichloro-substitution product of *butyrolactone*, into which it passes on reduction. The behaviour of succinyl chloride towards zinc ethide is in harmony with its lactone formula, for it then yields *γ-diethylbutyrolactone* (p. 428), and in the presence of benzene and aluminium chloride it chiefly affords *γ-diphenylbutyrolactone* (Ber. **24**, R. 320). A small quantity of *dibenzoylethane*, $C_6H_5CO{\cdot}CH_2CH_2{\cdot}COC_6H_5$, is produced at the same time. These reactions, whilst supporting the unsymmetrical formula, do not completely exclude the symmetrical representation (*cf.* Ber. **30**, 2268).

Similar considerations apply to the constitutional formula of phthalyl chloride in the aromatic series (see Vol. II).

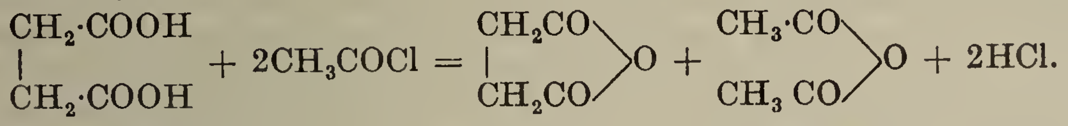
Pyrotartryl chloride, $C_5H_6O_2Cl_2$, b.p. 190–195° (Ber. **16**, 2624).

unsym.-*Dimethylsuccinyl chloride*, $C_6H_8O_2{\cdot}Cl_2$, b.p. 200–202° (Ann. **242**, 138, 207).

Anhydrides of the Succinic Acid Group

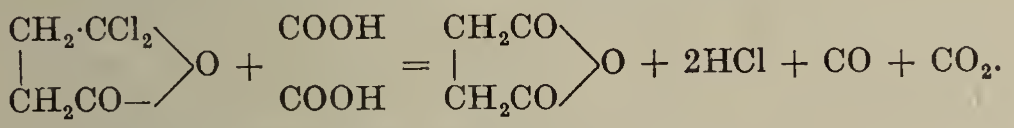
The ready formation of anhydride is characteristic of succinic acid and its alkyl derivatives. It proceeds the more easily the more hydrogen atoms are replaced by alcohol radicals.

Formation.—(1) By heating the acids alone. (2) By the action of P_2O_5 (Ber. **28**, 1289), PCl_5 or $POCl_3$ (Ann. **242**, 150) on the acids. (3) By treating the acids with the chloride or anhydride of a monobasic fatty acid, *e.g.* acetyl chloride or acetic anhydride (*Anschütz*, Ann. **226**, 1):



$$\begin{array}{l} CH_2{\cdot}COOH \\ | \\ CH_2{\cdot}COOH \end{array} + 2CH_3COCl = \left.\begin{array}{l} CH_2CO \\ | \\ CH_2CO \end{array}\right\rangle O + \left.\begin{array}{l} CH_3{\cdot}CO \\ \\ CH_3\ CO \end{array}\right\rangle O + 2HCl.$$

(4) When the chloride of a dicarboxylic acid acts (*a*) on the acid, or (*b*) on anhydrous oxalic acid (Ann. **226**, 6):



$$\left.\begin{array}{l} CH_2{\cdot}CCl_2 \\ | \\ CH_2CO- \end{array}\right\rangle O + \begin{array}{l} COOH \\ \\ COOH \end{array} = \left.\begin{array}{l} CH_2CO \\ | \\ CH_2CO \end{array}\right\rangle O + 2HCl + CO + CO_2.$$

Succinic anhydride, m.p. 120°, b.p. 261°.

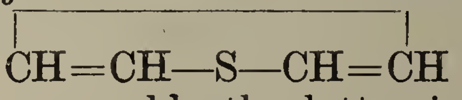
Methylsuccinic anhydride, pyrotartaric anhydride, m.p. 32°, b.p. 247° (Ann. **336**, 299: C. 1904, I. 1485). *Ethylsuccinic anhydride*, b.p. 243°. iso*Propylsuccinic anhydride*, b.p. 250°.

sym.-*Dimethylsuccinic anhydride*, *para-* m.p. 38°, *meso-* m.p. 87° (Ber. **26**, 1460: C. 1899, II. 610). sym.-*Methylethylsuccinic anhydride*, *meso-* b.p. 244°. sym.-*Diethylsuccinic anhydride*, *meso-* b.p. 245°. as-*Dimethylsuccinic anhydride*, m.p. 20°, b.p. 219°.

Trimethylsuccinic anhydride, m.p. 31°, b.p. 231°/760 mm., 101°/12 mm.

Tetramethylsuccinic anhydride, m.p. 147°, b.p. 231°. *Tetraethylsuccinic anhydride*, m.p. 86°, b.p. 270°. *Tetrapropylsuccinic anhydride*, m.p. 37°.

Properties and Reactions.—Succinic anhydride has a peculiar, faint, penetrating odour. It can be recrystallized from chloroform. It reverts to succinic acid in moist air, but more rapidly when boiled with water. It yields succinic alkyl ester acids with alcohols. Ammonia and amines change it to succinamic and alkyl succinamic acids. PCl_5 changes it to succinyl chloride. Sodium amalgam reduces it to butyrolactone (Ber. **29**, 1193); reduction of homologous succinic anhydrides by sodium and alcohol produces γ-lactones and even 1:4-glycols (*cf.* pp. 360, 425). If the anhydride is boiled for some time it loses CO_2 and changes to the dilactone of acetonediacetic acid, $CO(CH_2{\cdot}CH_2CO_2H)_2$ (*q.v.*); P_2S_3 converts succinic anhydride and sodium succinate into thiophen, $\overline{CH{=}CH{-}S{-}CH{=}CH}$ (*q.v.*). The homologues of succinic anhydride resemble the latter in behaviour.

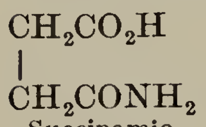


as-Dimethylsuccinic anhydride is partially decomposed by Al_2Cl_6 in chloroform into CO, H_2O, and dimethylacrylic acid, $(CH_3)_2C:CHCOOH$ (C. 1902, I. 567).

Peroxides.—*Succinyl peroxide*, $(C_4H_4O_4)$, is obtained from succinyl chloride and sodium peroxide. It is a very explosive crystalline powder (Ber. **29**, 1724). *Succinic peroxide*, $O_2(COCH_2CH_2COOH)_2$, m.p. 124° with decomposition, is prepared from succinic anhydride and 7·5 per cent. H_2O_2 solution. It explodes when heated, and decomposes in xylene solution into CO_2, a small quantity of adipic acid (p. 561), succinic anhydride, and other bodies. Water hydrolyses it into succinic acid and *succinic hydrogen peroxide*, $HOCOCH_2CH_2CO{\cdot}OOH$, m.p. 107° with decomposition, which decomposes on careful heating into CO_2, H_2O, and acrylic acid (C. 1904, II. 765).

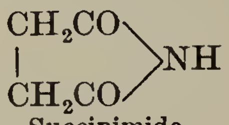
Nitrogen-containing Derivatives of the Succinic Acid Group

Succinic acid, like oxalic acid, yields an imide, a diamide, a nitrile acid and dinitrile:



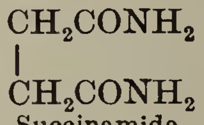
$$\begin{array}{l} CH_2CO_2H \\ | \\ CH_2CONH_2 \end{array}$$

Succinamic acid.



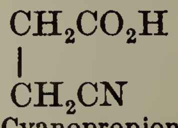
$$\begin{array}{l} CH_2CO \\ | \\ CH_2CO \end{array}\!\!>NH$$

Succinimide.



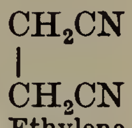
$$\begin{array}{l} CH_2CONH_2 \\ | \\ CH_2CONH_2 \end{array}$$

Succinamide.



$$\begin{array}{l} CH_2CO_2H \\ | \\ CH_2CN \end{array}$$

β-Cyanopropionic acid.

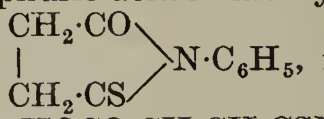


$$\begin{array}{l} CH_2CN \\ | \\ CH_2CN \end{array}$$

Ethylene cyanide.

(*a*) **Amic Acids** (Ann. **309**, 316).—Most of these have been prepared by decomposing the imides with alkalis or barium hydroxide. They are also formed on adding ammonia, primary aliphatic amines, and aromatic amines (*e.g.* aniline and phenyl-hydrazine) to acid anhydrides. They behave like oxamic acid (p. 538). When heated, or when treated with dehydrating agents, *e.g.* PCl_5 or CH_3COCl, they become converted into imides, which bear the same relation to them that the anhydrides sustain to the dicarboxylic acids.

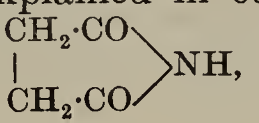
Succinamic acid, $CO_2H{\cdot}CH_2CH_2{\cdot}CONH_2$, is obtained from succinimide by the action of barium hydroxide solution. *Succinamic methyl ester*, m.p. 90°, is obtained from succinimide and methyl alcohol at 170° (C. 1899, II. 864). *Succinethylamic acid*, $CO_2H{\cdot}CH_2CH_2{\cdot}CONHC_2H_5$ (Ann. **251**, 319). *Succinanilic acid*, $CO_2HCH_2CH_2CONHC_6H_5$ (Ber. **20**, 3214); *methyl ester*, m.p. 98°, is obtained from succinanil (p. 553) and sulphuric acid in methyl alcoholic solution; P_2S_5 in toluene produces *thiosuccinanil*, $\begin{array}{l} CH_2{\cdot}CO \\ | \\ CH_2{\cdot}CS \end{array}\!\!>N{\cdot}C_6H_5$, m.p. 167°, which is split by alkalis into *thiosuccinanilic acid*, $HOCO{\cdot}CH_2CH_2CSNHC_6H_5$, m.p. 107° (Ber. **39**, 3303).



as-*Dimethylsuccinanilic acid*, $CO_2HC(CH_3)_2CH_2CONHC_6H_5$, m.p. 189°.

(*b*) **Imides.**—These are produced (1) on heating the acid anhydrides in a current of ammonia; (2) when the ammonium salts, diamides, and amic-acids are heated; (3) from the dinitriles, by partial hydration (C. 1902, I. 711). They show a symmetrical structure, as will be explained in connection with succinanil.

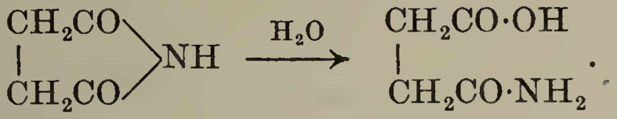
Succinimide, $\begin{array}{l} CH_2{\cdot}CO \\ | \\ CH_2{\cdot}CO \end{array}\!\!>NH$, m.p. 126°, b.p. 288°, crystallizes with



water, and has the character of an acid, as the hydrogen of the NH-group can be replaced by metals.

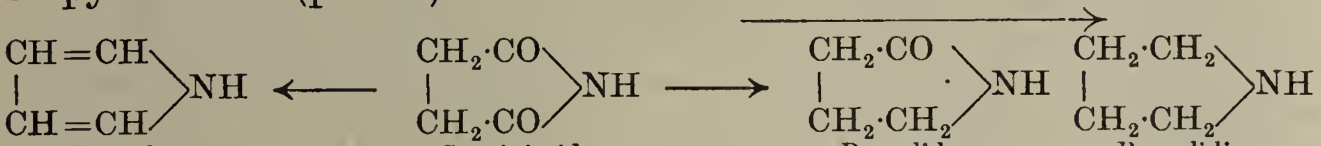
Potassium succinimide, $C_2H_4(CO)_2NK$; *sodium succinimide* (Ber. **28**, 2353); *silver succinimide* (Ann. **215**, 200); *potassium tetrasuccinimide tri-iodo-iodide*, $(C_4H_5O_2N)_4I_3{\cdot}KI$ (Ber. **27**, R. 478: **29**, R. 298).

The cyclic imides are readily broken down by alkalis and alkaline earths:



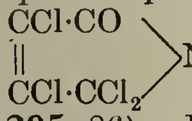
$$\left.\begin{array}{l}CH_2CO\\ |\\ CH_2CO\end{array}\right\rangle NH \xrightarrow{H_2O} \begin{array}{l}CH_2CO{\cdot}OH\\ |\\ CH_2CO{\cdot}NH_2\end{array}.$$

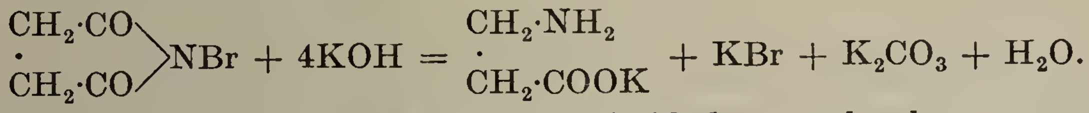
On distilling succinimide with zinc dust, pyrrole (p. 369) is formed; when heated with sodium in alcoholic solution it is converted into pyrrolidine (p. 386). Electrolytic reduction produces γ-butyrolactam or pyrrolidone (p. 450).



$$\left.\begin{array}{l}CH{=}CH\\ |\\ CH{=}CH\end{array}\right\rangle NH \longleftarrow \left.\begin{array}{l}CH_2{\cdot}CO\\ |\\ CH_2{\cdot}CO\end{array}\right\rangle NH \longrightarrow \left.\begin{array}{l}CH_2{\cdot}CO\\ |\\ CH_2{\cdot}CH_2\end{array}\right\rangle NH \quad \left.\begin{array}{l}CH_2{\cdot}CH_2\\ |\\ CH_2{\cdot}CH_2\end{array}\right\rangle NH$$

Pyrrole. Succinimide. Pyrrolidone. Pyrrolidine.

Hypochlorous acid, and hypobromous acid acting on succinimide, and iodine on silver succinimide produce: *succinochloride*, $C_2H_4(CO)_2NCl$, m.p. 148°; *succinobromimide*, $C_2H_4(CO)_2NBr$, m.p. 174° with decomposition, and *succiniodoimide* (Ber. **26**, 985). Phosphorus pentachloride converts succinimide into dichloromaleinimide chloride,  $\left.\begin{array}{l}CCl{\cdot}CO\\ \|\\ CCl{\cdot}CCl_2\end{array}\right\rangle NH$, pentachloropyrrole, C_4Cl_5N, and the heptachloride, C_4Cl_7N (Ann. **295**, 86). Bromine and potassium hydroxide convert succinimide into β-aminopropionic acid (p. 448):



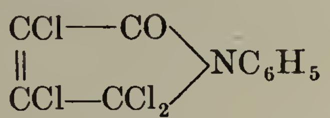
$$\left.\begin{array}{l}CH_2{\cdot}CO\\ \cdot\\ CH_2{\cdot}CO\end{array}\right\rangle NBr + 4KOH = \begin{array}{l}CH_2{\cdot}NH_2\\ \cdot\\ CH_2{\cdot}COOK\end{array} + KBr + K_2CO_3 + H_2O.$$

Sodium methoxide changes succinobromimide by a molecular rearrangement into *carbomethoxy-β-aminopropionic ester*, $CH_3O{\cdot}CO{\cdot}NHCH_2CH_2CO_2CH_3$, m.p. 33·5° (Ber. **26**, R. 935).

Succinmethylimide, $C_2H_4(CO)_2N{\cdot}CH_3$, m.p. 66·5°, b.p. 234°, is obtained from the oxime of lævulinic acid (p. 477) by a Beckmann transformation under the action of concentrated sulphuric acid (Ann. **251**, 318).

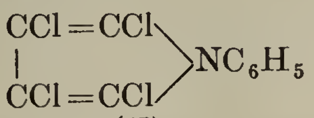
Succinethylimide, m.p. 26°, b.p. 234°, is formed when ethyl iodide acts on potassium succinimide. It yields ethylpyrrole when it is distilled with zinc dust. *Succinisopropylimide*, m.p. 61°, b.p. 230°. *Succinisobutylimide*, m.p. 28°, b.p. 247° (Ber. **28**, R. 600).

Phenyl succinimide, succinanil, $C_2H_4(CO)_2{\cdot}N{\cdot}C_6H_5$, m.p. 150°, is converted by PCl_5 into dichloromaleic anil dichloride (I), the lactam of γ-anilidoperchlorocrotonic acid and tetrachlorophenylpyrrole (II). This last fact, and the reduction of dichloromaleic dichloride to γ-anilidobutyrolactam or *N*-phenyl butyrolactam (III), indicate that the symmetrical formula properly represents both succinanil and succinimide (Ann. **295**, 39, 88).



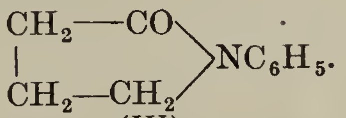
$$\left.\begin{array}{l}CCl{-}{-}CO\\ \|\\ CCl{-}{-}CCl_2\end{array}\right\rangle NC_6H_5$$

(I)



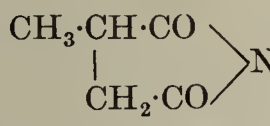
$$\left.\begin{array}{l}CCl{=}CCl\\ |\\ CCl{=}CCl\end{array}\right\rangle NC_6H_5$$

(II)



$$\left.\begin{array}{l}CH_2{-}{-}CO\\ |\\ CH_2{-}{-}CH_2\end{array}\right\rangle NC_6H_5.$$

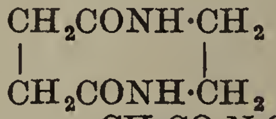
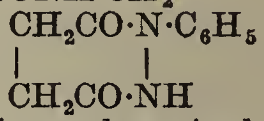
(III)

Pyrotartrimide,  $\left.\begin{array}{l}CH_3{\cdot}CH{\cdot}CO\\ |\\ CH_2{\cdot}CO\end{array}\right\rangle NH$, m.p. 66°. *N*-Alkylpyrotartrimides (Ber. **30**, 3039). sym.-*Dimethylsuccinimide* (Ber. **22**, 646). as-*Dimethylsuccinimide*, m.p. 106°, is obtained by heating αα-dimethylsuccinonitrile acid (C. 1899, I. 873); also by oxidation of mesitylic acid (Ann. **242**, 208: Ber. **14**, 1075). as-*Dimethylsuccinanil*, m.p. 85°. *Trimethylsuccinanil*, m.p. 129°. *Tetramethylsuccinanil*, m.p. 88° (Ann. **285**, 234: **292**, 176, 184). iso*Propylsuccinimide*, m.p. 60° (Ann. **220**, 276).

(*c*) **Diamides and Hydrazides.**—*Succinamide*, $NH_2CO\cdot CH_2CH_2CONH_2$, is produced like oxamide. It crystallizes from hot water in needles. At 200° it decomposes into ammonia and succinimide. *Succinodibromodiamide*, $NH_2CO\cdot[CH_2]_2CONBr_2$, is obtained from succinamide and KBrO (see also β-Lactyl urea, p. 500).

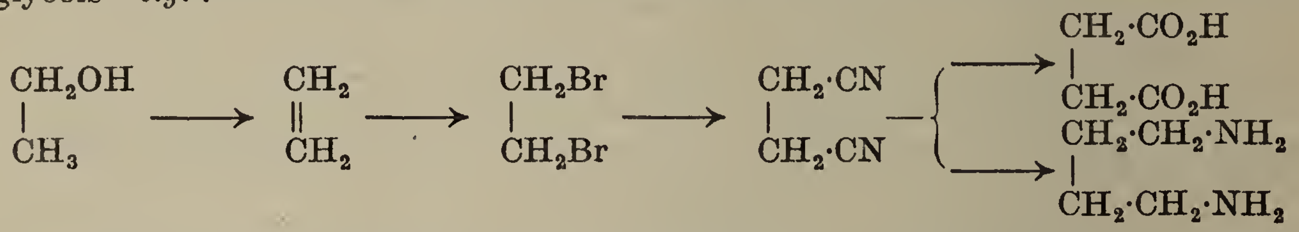
Pyrotartramide, m.p. 225° (Ber. **29**, R. 509).

Succinohydrazide, $(\cdot CH_2CO\cdot NHNH_2)_2$, m.p. 167° (J. pr. Chem. [2] **51**, 190 : Ber. **39**, 3376).

(*d*) **Cyclic Diamides.**—*Succinethylenediamide*,  $\begin{array}{l} CH_2CONH\cdot CH_2 \\ |\qquad\qquad\quad | \\ CH_2CONH\cdot CH_2 \end{array}$ (Ber. **27**, R. 589). *Succinophenylhydrazide*, 1-*phenyl*-3 : 6-*pyridazone*,  $\begin{array}{l} CH_2CO\cdot N\cdot C_6H_5 \\ |\qquad\qquad | \\ CH_2CO\cdot NH \end{array}$, m.p. 199°, is obtained from the hydrochloride of phenylhydrazine and succinyl chloride (Ber. **26**, 674, 2181) ; succinic anhydride and phenylhydrazine yield the isomeric N-*anilinosuccinimide*, $C_2H_4(CO)_2N\cdot NHC_6H_5$, m.p. 155°.

(*e*) **Nitrilic Acids and Dinitriles.**—*Dimethylcyanopropionic ester*, $CN\cdot CH_2\cdot C(CH_3)_2CO_2C_2H_5$, b.p. 218°, results when dimethyl cyanosuccinic mono-ethyl ester is heated (C. 1899, I. 874).

Dinitriles are produced from alkylene bromides by treatment with potassium cyanide. Absorption of water converts these dinitriles into the ammonium salts of the corresponding acids, the synthesis of which they thus facilitate. When reduced, they take up eight atoms of hydrogen and become the diamines of the glycols—*e.g.* :

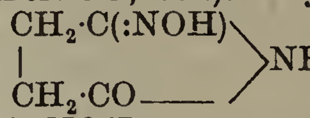
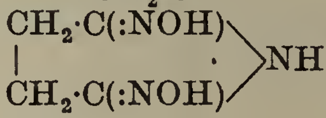

$$\begin{array}{l} CH_2OH \\ | \\ CH_3 \end{array} \longrightarrow \begin{array}{l} CH_2 \\ \| \\ CH_2 \end{array} \longrightarrow \begin{array}{l} CH_2Br \\ | \\ CH_2Br \end{array} \longrightarrow \begin{array}{l} CH_2\cdot CN \\ | \\ CH_2\cdot CN \end{array} - \left\{ \begin{array}{l} \longrightarrow \begin{array}{l} CH_2\cdot CO_2H \\ | \\ CH_2\cdot CO_2H \end{array} \\ \longrightarrow \begin{array}{l} CH_2\cdot CH_2\cdot NH_2 \\ | \\ CH_2\cdot CH_2\cdot NH_2 \end{array} \end{array} \right.$$

Succinonitrile, *ethylene cyanide*, $CN\cdot CH_2CH_2\cdot CN$, m.p. 54·5°, b.p. 159°/20 mm., is an amorphous, transparent mass (C. 1901, II. 807), readily soluble in water, chloroform and alcohol, but sparingly soluble in ether. It is also obtained by the electrolysis of potassium cyanacetate (p. 544).

It yields succinic acid when saponified, and tetramethylene diamine upon reduction. It combines with 4HI (Ber. **25**, 2543). Paraformaldehyde, glacial acetic acid and sulphuric acid convert it into methylene succinimide, $(C_2H_4\cdot C_2O_2N)_2CH_2$, m.p. above 270° (J. pr. Chem. [2] **50**, 3). When heated with water and sulphuric acid it forms succinimide (C. 1902, I. 711).

Pyrotartaric nitrile, m.p. 12°, is obtained from allyl iodide and two molecules of KNC (Ann. **182**, 327 : Ber. **28**, 2952).

as-*Dimethylsuccinic nitrile*, $CN\cdot CH_2C(CH_3)_2CN$, b.p. 219° (Ber. **22**, 1740).

(*f*) **Oximes.**—*Succinyl hydroxamic acid*, $CO_2H\cdot CH_2CH_2\cdot C(:N\cdot OH)OH$ (Ber. **28**, R. 999). *Succinyl hydroxamic tetracetate*, m.p. 130° (Ber. **28**, 754). Hydroxylamine converts succinonitrile into *succinimidoxime*,  $\begin{array}{l} CH_2\cdot C(:NOH) \\ |\qquad\qquad\qquad\quad \\ CH_2\cdot CO \end{array}\!\!>\!NH$, m.p. 197° (Ber. **24**, 3427), and *succinimide dioxime*,  $\begin{array}{l} CH_2\cdot C(:NOH) \\ | \\ CH_2\cdot C(:NOH) \end{array}\!\!>\!NH$, m.p. 207° (Ber. **22**, 2964).

Halogen Substitution Products of the Succinic Acid Group

The **monosubstitution products** are obtained (1) by the direct action of halogens on the acids, their esters, chlorides or anhydrides. In case of the acids it is advisable to act on them with amorphous phosphorus and bromine (Ber. **21**, R. 5) ; (2) by the addition of a halogen hydride to the corresponding unsaturated dicarboxylic acid of the fumaric and maleic groups (Ann. **254**, 161) ; (3) by the action of a halogen hydride, and (4) of PCl_5 or PBr_5 on the corresponding α-monohydroxydicarboxylic acids (Ann. **130**, 21) ; (5) from aminosuccinic acids by means of potassium bromide, sulphuric acid, bromine and nitric oxide (Ber. **28**, 2769).

Inactive *chlorosuccinic acid*, $CO_2H \cdot CHClCH_2 \cdot CO_2H$, m.p. 152°, is formed from fumaric acid and hydrochloric acid: *dimethyl ester*, b.p. 106·5°/14 mm.; *diethyl ester*, b.p. 122°/15 mm.; *anhydride*, m.p. 41°, b.p. 126°/12 mm. (Ann. **254**, 156: Ber. **23**, 3757).

dextrorotatory-(+)-*Chlorosuccinic acid*, m.p. 176° (decomp.), is obtained from *l*-malic acid and phosphorus pentachloride, a Walden inversion taking place (Kuhn, Ber. **61**, 509). Its silver salt yields *d*-malic acid when boiled with water: *dimethyl ester*, b.p. 107°/15 mm.; *chloride*, b.p. 92°/11 mm.; *anhydride*, b.p. 138°/20 mm. (Ber. **28**, 1289).

lævorotatory-(−)-*Chlorosuccinic acid* is prepared from *l*-aspartic acid, which can be changed to *l*-malic acid. Starting, therefore, with *l*-aspartic acid, it is not only possible to prepare (−)-chlorosuccinic acid and *l*-malic acid, but with the aid of the latter we can obtain (+)-chlorosuccinic acid, which can be transposed into *d*-malic acid (p. 605):

$$\begin{tikzcd}
 & \text{(−)-Chlorosuccinic acid} \arrow[dd] & d\text{-Malic acid.} \arrow[l] \\
l\text{-Aspartic acid} \arrow[ur] \arrow[dr] & & \\
 & l\text{-Malic acid} \arrow[r] & \text{(+)-Chlorosuccinic acid.} \arrow[uu]
\end{tikzcd}$$

On the other hand, (−)-chloro- and (−)-bromo-succinic acid, which yield *l*-malic acid with silver oxide, give, with ammonia, *d*-aminosuccinic acid, from which *d*-malic acid can be obtained on boiling the substance with barium hydroxide solution (*Walden Inversion*, pp. 70, 443) (Ber. **30**, 2795):

$$\begin{tikzcd}
\text{(−)-Chlorosuccinic acid} \arrow[r] \arrow[d] & l\text{-Malic acid} \\
d\text{-Aminosuccinic acid} \arrow[r] & d\text{-Malic acid.}
\end{tikzcd}$$

Inactive *bromosuccinic acid*, $CO_2H \cdot CHBrCH_2 \cdot CO_2H$, m.p. 160°, is prepared from hydrobromic acid and fumaric acid. It is decomposed by alkalis into these components (Ann. **348**, 261); *dimethyl ester*, b.p. 110°/10 mm.; *anhydride*, m.p. 31°, b.p. 137°/11 mm.

(+)-*Bromosuccinic dimethyl ester* is formed from *l*-malic acid and PBr_5, b.p. 124°/20 mm. (Ber. **28**, 1291).

(−)-*Bromosuccinic acid* is prepared from *l*-aspartic acid (Ber. **28**, 2770: **29**, 1699), m.p. 173° (decomp.).

Monoiodosuccinic acid has only been obtained as a basic lead salt (Ber. **30**, 200).

The free, inactive acids and their esters, when heated at the ordinary pressure, break down into a halogen acid and fumaric acid and its ester, whilst the anhydrides yield the halogen hydride and maleic anhydride (Ann. **254**, 157). Moist silver oxide converts bromosuccinic acid into inactive malic acid (*q.v.*), which can thus be synthesized in this way.

The addition of a halogen acid to ita-, citra-, and mesaconic acids (p. 571) produces chloropyrotartaric acids, $C_5H_7ClO_4$: (1) *Itachloropyrotartaric acid*, $CH_2 \cdot Cl \cdot CH(COOH) \cdot CH_2(COOH)$, m.p. 140–141° (*cf.* Paraconic acid and Itamalic acid). (2) *Mesa-* or *Citrachloropyrotartaric acid*, $CH_3 \cdot CCl(COOH) \cdot CH_2(COOH)$, m.p. 129° (Ann. **188**, 51: C. 1899, I. 1070).

Bromopyrotartaric acids, $C_5H_2BrO_4$: (1) *itabromopyrotartaric acid*, m.p. 137°; (2) *citrabromopyrotartaric acid*, m.p. 148°.

Dihalogen substitution products are produced (1) by the direct action of bromine and water on the acids; (2) by the addition of halogen acids to the monohalogen unsaturated acids of the fumaric and maleic series; (3) by the addition of halogens—particularly bromine—to the unsaturated acids of the fumaric and maleic series.

When hydrobromic acid is added to fumaric and maleic acids they yield the same monobromosuccinic acid, but with bromine, fumaric acid forms the sparingly soluble dibromosuccinic acid, whilst maleic acid and bromine yield the easily soluble *iso*dibromosuccinic acid and fumaric acid. These two dibromosuccinic acids have the same structural formula, they are symmetrical in arrangement, and their isomerism is probably due to the same cause prevailing with the *sym.*-dialkylsuccinic acids (p. 549). Yet they are intimately related to racemic and mesotartaric acids, which were first synthetically prepared by means of the dibromosuccinic acids. Inasmuch as fumaric acid yields racemic acid when oxidized, therefore the sparingly soluble dibromosuccinic acid, the dibromo-addition product of fumaric acid, should correspond with racemic acid, and *iso*dibromosuccinic acid with mesotartaric acid. However, the reactions of the dibromosuccinic acids show many contradictions.

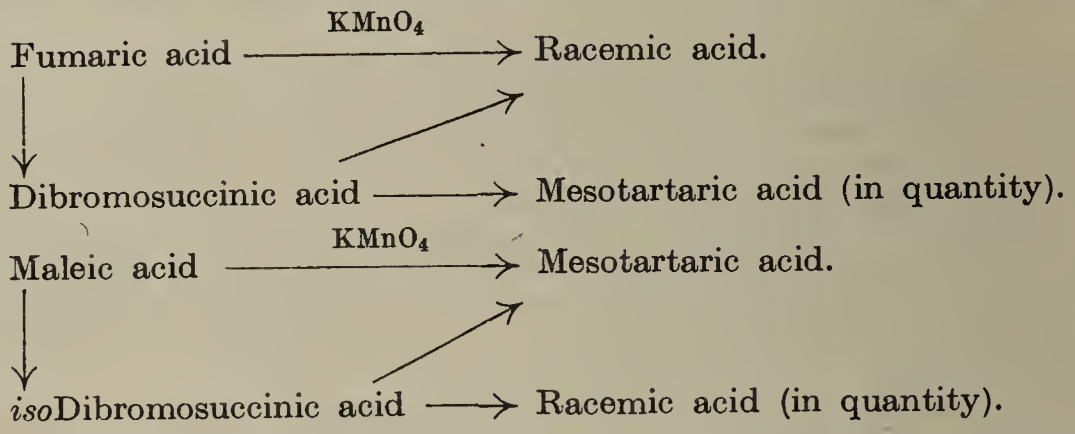
Dichlorosuccinic acid, m.p. 215° (decomp.), is prepared from fumaric acids and liquid chlorine; *methyl ester*, m.p. 32° (Ann. **280**, 210).

iso*Dichlorosuccinic acid*, m.p. 170° (decomp.), is obtained from the *anhydride*, m.p. 95°, the addition product of maleic anhydride and liquid chlorine. When heated, the anhydride changes to chloromaleic anhydride (Ann. **280**, 216).

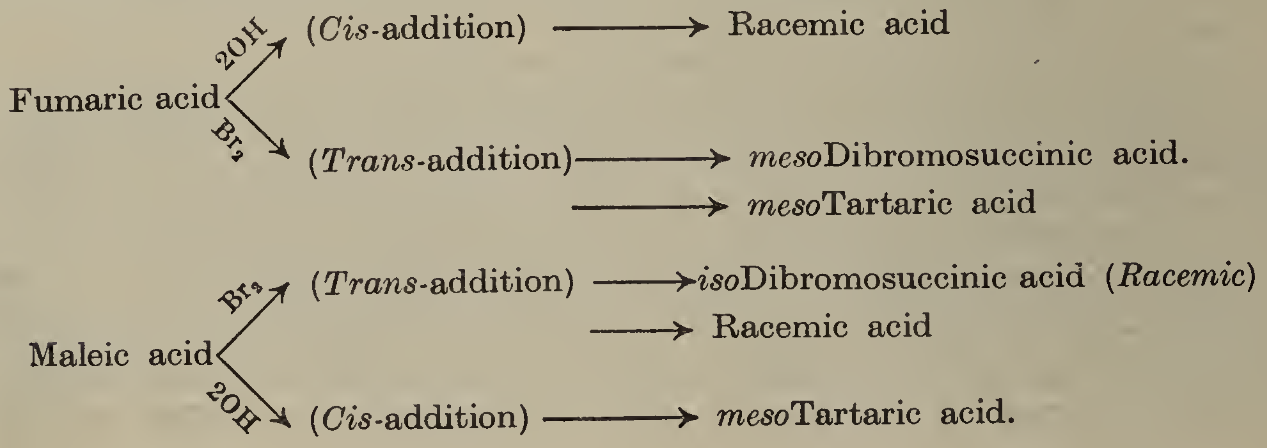
Dibromosuccinic Acids.—The *meso*-form (J.C.S. **101**, 1196) is obtained from fumaric acid and bromine. It is sparingly soluble and decomposes at 200–235° into hydrogen bromide and bromomaleic acid. When heated with acetic anhydride, it forms bromomaleic anhydride and acetyl bromide. *Methyl ester*, m.p. 62°; *ethyl ester*, m.p. 68°.

iso*Dibromosuccinic acid*, m.p. 166°, is formed from maleic acid and bromine in ethereal solution. It is a racemic compound and has been resolved by the use of morphine (J.C.S. **101**, 1196). *l*-Acid, m.p. 157°, $[\alpha]_D$ (in ethyl acetate) − 148°. Its *esters* are liquids. Its *anhydride*, $C_2H_2Br_2(CO)_2O$, m.p. 42°, is formed from maleic anhydride and bromine. At 100° it breaks down into HBr and bromomaleic anhydride (Ann. **280**, 207). *Anilic acid*, m.p. 144°: *anil*, m.p. 177° (Ann. **292**, 233: **239**, 143). When reduced, both acids yield succinic acid; when boiled with potassium iodide they change to fumaric acid, whilst boiling sodium hydroxide or barium hydroxide solutions convert them into acetylene dicarboxylic acid (Ann. **272**, 127). The sparingly soluble dibromo-acid, when boiled with 20 parts of water, passes into bromomaleic acid, whilst the readily soluble acid, under like treatment, becomes converted into bromofumaric acid. Two hundred parts of boiling water convert the difficultly soluble dibromo-acid into mesotartaric acid, together with a little racemic acid, whilst the readily soluble acid yields much racemic acid and but little of the mesotartaric acid (Ann. **292**, 295: **300**, 1).

The silver salt of the difficultly soluble dibromo-acid changes on boiling with water to mesotartaric acid (*q.v.*), whilst racemic acid is obtained under similar conditions from the salt of the easily soluble *iso*dibromosuccinic acid (Ber. **21**, 268). Much mesotartaric acid with but little racemic acid is formed on boiling the barium or calcium salt of the difficultly soluble dibromosuccinic acid. The contradictions in these reactions are made clearer in the scheme which follows:



The experiments of McKenzie lead to the conclusion that the explanation of these results is to bc found in the fact that the addenda (2Br or 2OH) add themselves differently to the double linkage, and the relationship between the various compounds is better expressed by the scheme—



It must not be assumed that the addition takes place in identical fashion with all unsaturated compounds. The course of the reaction depends so much on the constitution of the starting compound and the nature of the addenda that a prophecy of the resulting products, formed by the formation of two new asymmetric carbon atoms, is as unjustified as the prophecy of the configuration of a compound formed by substitution at an asymmetric carbon atom. The only certain method of determination depends upon the optical resolution of one of the addition products.

Trichlorosuccinic acid is a crystalline, exceedingly soluble mass, obtained on exposing chloromaleic acid, water and liquid chlorine to sunlight (Ann. **280**, 203).

Tetrachlorosuccinanil, m.p. 157°, is formed together with dichloromaleic anil chloride (p. 570), when PCl_5 acts on dichloromaleic anil (Ann. **295**, 33).

Tribromosuccinic acid, $C_2HBr_3(CO_2H)_2$, m.p. 136°, is produced when bromine and water act on bromomaleic acid and *iso*bromomaleic acid. The aqueous solution decomposes at 60° into CO_2, HBr, and dibromoacrylic acid, $C_3H_2Br_2O_2$ (p. 342). Alkalis convert it into dibromomaleic acid; whilst excess of ammonia produces monobromofumaric acid (Ann. **348**, 264).

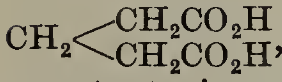
Dibromopyrotartaric Acids.—The addition of bromine, to ita-, citra-, and mesaconic acids gives rise to three dibromopyrotartaric acids, which upon reduction revert to the same pyrotartaric acid (p. 548).

The *ita-*, *citra-*, and *mesa-dibromopyrotartaric acids*, $C_5H_6Br_2O_4$, are distinguished by their different solubility in water. The *ita-* compound changes to aconic acid, $C_5H_4O_4$, when the solution of its sodium salt is boiled; the *citra-* and *mesa-* compounds, on the other hand, yield bromomethacrylic acid (p. 345).

An excess of potassium hydroxide will convert *citra*dibromopyrotartaric acid into bromomesaconic acid (p. 572).

Glutaric Acid Group

Glutaric acid and its alkyl derivatives, like succinic acid, are characterized by the fact that when heated they break down into the anhydride and water. The anhydrides readily yield anilic acids, from which anils can be obtained by the withdrawal of water. The glutaric acids resemble the succinic acids in behaviour, but they are changed to anhydrides with greater difficulty by acetyl chloride, and are not so volatile with steam.

Glutaric acid (*normal pyrotartaric acid*) [pentane diacid]  $CH_2{<}\begin{matrix}CH_2CO_2H\\CH_2CO_2H\end{matrix}$, m.p. 97°, is isomeric with methylsuccinic acid or pyrotartaric acid, as well as with ethyl- and dimethyl-malonic acids (p. 546). It was first obtained by the reduction of α-hydroxyglutaric acid with hydriodic acid. It may be synthetically prepared from trimethylene bromide (p. 372), through the cyanide; from acetoacetic ester by means of the acetoglutaric ester (*q.v.*); from glutaconic acid by reduction (p. 575), and from propanetetracarboxylic acid or methylene dimalonic acid, $C_3H_4(CO_2H)_4$, by the removal of $2CO_2$; from hydroresorcinol and potassium hypobromite (Ber. 32, 1871); by electrolysis of a mixture of potassium malonic ester and succinic ester (C. 1903, II. 1053). Glutaric acid crystallizes in large monoclinic plates, and distils near 303°, with scarcely any decomposition. It is soluble in 1·2 parts water at 14°.

The *calcium salt*, $C_5H_6O_4Ca + 4H_2O$, and *barium salt*, $C_5H_6O_4Ba + 5H_2O$, are easily soluble in water; the first is more readily in cold than in warm water (like calcium butyrate, p. 304).

Monomethyl ester, b.p. 153°/20 mm.; *dimethyl ester*, b.p. 214° (Ber. **26**, R. 276: C. 1900, I. 169); *ethyl ester*, b.p. 237°.

The *anhydride*, $C_5H_6O_3$, m.p. 56–57°, forms on slowly heating the acid to 230–280°, and in the action of acetyl chloride on the silver salt of the acid.

Glutarimide, $C_3H_6(CO)_2NH$, m.p. 152°, is formed when ammonium glutarate is heated; when trimethylene cyanide (*q.v.*) is heated with sulphuric acid and water to 180–200° (C. 1902, I. 711), and by oxidation of pentamethyleneimine (p. 386) or piperidine with H_2O_2 (Ber. **24**, 2777). When heated to redness with zinc dust, a little pyridine is formed (Ber. **16**, 1883).

Glutaric peroxide, $O_2(COCH_2CH_2CH_2COOH)_2$, m.p. 108° (decomp.), is prepared from glutaric anhydride and H_2O_2. On being heated it yields a little suberic acid (p. 562) (C. 1904, II. 766).

Glutaric dihydrazide, $(CH_2)_3(CONHNH_2)_2$, m.p. 176°. *Glutaric diazide* is an explosive oil (J. pr. Chem. [2] **62**, 194).

Nitrile of glutaric acid, trimethylene cyanide, $CN\cdot[CH_2]_3\cdot CN$, m.p. − 29°, b.p. 286° (C. 1901, II. 807), is obtained from trimethylene bromide and potassium cyanide. Alcohol and sodium convert it into pentamethylene diamine (p. 385) and piperidine (p. 386), whilst it yields glutarimide dioxime with hydroxylamine (Ber. **24**, 3431).

β-Chloroglutaric acid is obtained from β-hydroxyglutaric acid. Diethylaniline converts it into glutaconic acid (p. 575) (C. 1905, I. 1225).

Pentachloroglutaric acid, $CO_2H\cdot CCl_2CHClCCl_2\cdot CO_2H$ (Ber. **25**, 2219).

α-Bromo- and *α-iodo-glutaric ester* are converted by KOH or diethyl aniline into trimethylene dicarboxylic acid (C. 1905, I. 1225).

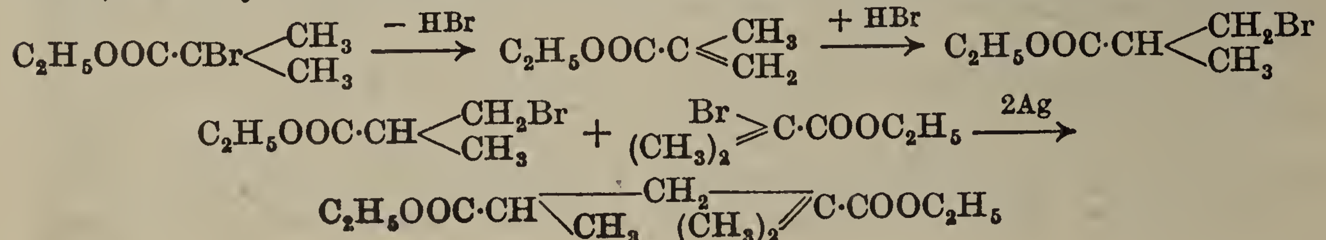
αγ-Dibromoglutaric acid, $CH_2(CHBrCOOH)_2$, *cis*-form, m.p. 170°; *trans*-form, m.p. 143° (decomp.) (*cf.* p. 559, αγ-di-alkylglutaric acids) result when glutaric acid is brominated, and by the oxidation of *cis*- and *trans*-dibromides of *cyclo*pentadiene (Vol. II). Reduction converts them into glutaric acid, whilst *αβ-dibromoglutaric acid*, the dibromide of glutaconic acid (p. 575), yields glutaconic acid when reduced (Ann. **314**, 307, 509).

Mono-alkylglutaric Acids.—*α-Methylglutaric acid*, $COOH\cdot CH_2\cdot CH_2\cdot CHMe\cdot COOH$, m.p. 76°, results from the reduction of saccharone, and on treating camphorphorone with $KMnO_4$ (Ber. **25**, 265). It may be synthesized from methylacetoacetic ester and β-iodopropionic acid; and when KNC acts on lævulinic acid. It is a by-product in the decomposition of *iso*butanetricarboxylic ester, the condensation product of bromo*iso*butyric ester and alcoholic sodium malonate (see below). A series of α-alkylglutaric acid are formed by the decomposition of the alkylpropane-ααγ-tricarboxylic esters (C. 1901, I. 302). α-Methylglutaric acid and P_2S_5 yield 3-methylpenthiophen. *Anhydride*, m.p. 40°, b.p. 283°; *anilic acid* (Ann. **292**, 211); *dinitrile*, *α-methyltrimethylene cyanide*, b.p. 270°, is prepared from dibromobutane and KNC (C. 1902, II. 1097).

α-Ethylglutaric acid, m.p. 60°, b.p. 195°/30 mm.; *anhydride*, b.p. 275°; *anilic acid* (Ann. **292**, 144, 215).

β-Methylglutaric acid, $CH_3CH(CH_2CO_2H)_2$, m.p. 86°, is formed from crotonic ester and sodium malonic ester or sodium cyanoacetic ester (C. 1906, I. 186); also from ethylidene dimalonic acid; *anhydride*, m.p. 46°, b.p. 283° (Ber. **24**, 2888). *β-Ethylglutaric acid*, m.p. 67°, is prepared from propylidene dimalonic acid. *β-*iso*Propylglutaric acid*, m.p. 100°, is formed from α-cyano-β-*iso*propylglutaric mono-ester or carboxy-β-*iso*propylglutaric ester, whose methyl-substitution product yields *α-methyl-β-*iso*propylglutaric acid* (Ber. **38**, 947). The β-*iso*propylglutaric acid, when oxidized with CrO_3, is converted into terpenylic acid (p. 612); but $KMnO_4$ produces terebic acid (p. 612) (C. 1899, I. 1157: 1900, II. 39, 467). The *dinitriles* of the β-alkylglutaric acids are obtained also by boiling with water the oximes of alkylidene bis-pyroracemic acids (diketopimelic acids), $RCH[CH_2C(NOH)COOH]_2$ (C. 1906, I. 1105).

Di- and Tri-alkylglutaric acids are produced together with tri- and tetramethyl succinic acids in the syntheses of these latter acids from α-bromo*iso*butyric acid with silver, with methylmalonic ester, etc. In order to explain the formation of these unexpected alkylglutaric acids in these reactions, it has been assumed that a portion of the α-bromo*iso*butyric acid gives up HBr and passes into methacrylic ester. In the silver reaction the HBr attaches itself to the methyl acrylic ester, and the silver withdraws bromine from the α- and β-bromo*iso*butyric esters, whereby the residues unite to trimethylglutaric ester (Ber. **22**, 48, 60):

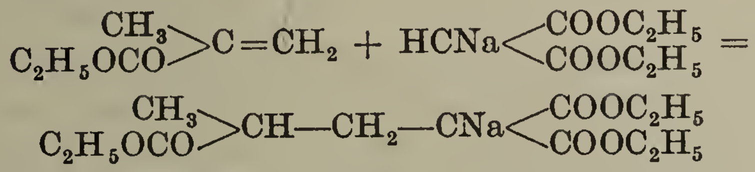


$$C_2H_5OOC\cdot CBr\Big<\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix} \xrightarrow{-\,HBr} C_2H_5OOC\cdot C\Big\lessgtr\begin{smallmatrix}CH_3\\CH_2\end{smallmatrix} \xrightarrow{+\,HBr} C_2H_5OOC\cdot CH\Big<\begin{smallmatrix}CH_2Br\\CH_3\end{smallmatrix}$$

$$C_2H_5OOC\cdot CH\Big<\begin{smallmatrix}CH_2Br\\CH_3\end{smallmatrix} + \begin{smallmatrix}Br\\(CH_3)_2\end{smallmatrix}\Big>C\cdot COOC_2H_5 \xrightarrow{2Ag}$$

$$C_2H_5OOC\cdot CH\begin{smallmatrix}\text{——}CH_2\text{——}\\ CH_3 \quad (CH_3)_2\end{smallmatrix}C\cdot COOC_2H_5$$

In the second reaction sodium methylmalonic ester attaches itself to methyl acrylic ester, and when the addition product is saponified it yields dimethyl glutaric acid (Ber. **24**, 1041, 1923):



$$\begin{matrix}\mathrm{CH_3}\\\mathrm{C_2H_5OCO}\end{matrix}\!\!>\mathrm{C{=}CH_2} + \mathrm{HCNa}<\!\!\begin{matrix}\mathrm{COOC_2H_5}\\\mathrm{COOC_2H_5}\end{matrix} =$$

$$\begin{matrix}\mathrm{CH_3}\\\mathrm{C_2H_5OCO}\end{matrix}\!\!>\mathrm{CH{-}CH_2{-}CNa}<\!\!\begin{matrix}\mathrm{COOC_2H_5}\\\mathrm{COOC_2H_5}\end{matrix}$$

The αα′- (or αγ-) and αβ-dialkyl glutaric acids, similarly to the *sym.*-dialkyl succinic acids (p. 549), exist in two modifications—the *racemic*- and *meso*-forms.

αα′-Dimethylglutaric acid, $CH_2[CH(CH_3)CO_2H]_2$, m.p. *meso*-acid, 127°, *racemic*-acid, 140° (Ann. **292**, 146: Ber. **29**, R. 421), is also prepared from CH_2I_2 and sodium α-cyanopropionic ester. The *meso*-acid can also be obtained by reduction of αα-dimethylglutaconic acid (p. 577) by means of HI and phosphorus, accompanied by the wandering of a methyl group (C. 1903, I. 697).

Bromine converts both acids into α-bromo-derivatives, from which hydroxy-dimethyl glutaric acids and their lactones are obtained (Ber. **25**, 3221: Ann. **292**, 146). The 127° acid is converted by acetyl chloride or acetic anhydride into the *anhydride*, m.p. 94°, while the 140° acid is unaffected at moderate temperatures (Ber. **31**, 2112). The 140° acid is the *racemic* form and has been resolved by the use of strychnine or brucine (Ber. **43**, 3250: C. 1919, I. 607).

αα′-Diethylglutaric acids, m.pp. 120° and 94°, are formed by the reduction of β-hydroxy-αα′-diethylglutaric acid by hydriodic acid (C. 1902, II. 107). On heating the barium salts of αα′-dimethyl and -diethylglutaric acids there result dimethyl- and diethyl-*cyclo*pentanone (C. 1897, II. 342). *αα′-Methyl*iso*butyl-glutaric acids*, m.pp. 121° and 78°, are produced from sodium *iso*butylmalonic ester and bromo*iso*butyric ester, etc. (C. 1900, II. 368).

αβ-Dimethylglutaric acids, $CO_2H{\cdot}CH(CH_3)CH(CH_3)CH_2CO_2H$, *trans*-acid fluid, *cis*-acid, m.p. 87°, are formed by hydrolysis and splitting off of CO_2 from the condensation products of crotonic ester, sodium cyanoacetic ester and iodomethane; also of angelic or tiglic esters (p. 346) and sodium cyanoacetic ester (C. 1903, I. 565, 1122: 1906, I. 186: *cf.* also Ann. **292**, 147: Ber. **29**, 2058).

as-*αα-Dimethylglutaric acid*, $CO_2H{\cdot}C(CH_3)_2CH_2CH_2CO_2H$, m.p. 85°; *anhydride*, m.p. 38°, is prepared from γ-chloro*iso*butylacetic acid and potassium cyanide (C. 1898, II. 963: *cf.* C. 1902, II. 25); by reduction of the addition product of HI to αα-dimethylglutaconic acid by means of zinc and hydrochloric acid; also by oxidation of camphor derivatives (Vol. II) (C. 1900, II. 282). Treatment of αα-dimethylglutaric anhydride with Al_2Cl_6 in chloroform leads to a partial production of *iso*caprolactone and pyroterebic acid and CO_2 (*cf.* as-dimethyl-succinic anhydride (p. 552); also C. 1902, I. 567).

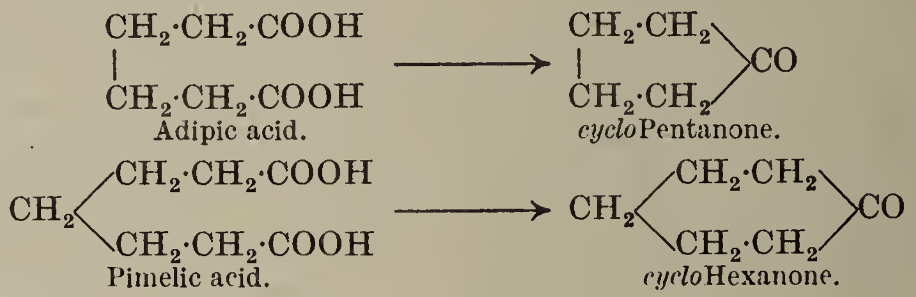
ββ-Dimethylglutaric acid, $CO_2H{\cdot}CH_2C(CH_3)_2CH_2CO_2H$, m.p. 104°; *anhydride*, m.p. 124°, is prepared from dimethylacrylic ester with sodium or potassium malonic ester with subsequent decomposition of the dimethylpropanetricarboxylic ester which is formed (Ann. **292**, 145: C. 1897, I. 28); by decomposition of ββ-dimethylpropanetetracarboxylic ester (C. 1899, I. 926); of ββ-dimethyl-αα′-dicyanoglutaric ester or imide (C. 1901, I. 821); also by oxidation, by means of KBrO, of dimethylhydroresorcinol (Vol. II) (C. 1906, II. 18: Ber. **32**, 1879); *anilic acid*, m.p. 174°. Bromo-ββ-dimethylglutaric ester and alcoholic potassium hydroxide yield the two caronic acids (Vol. II). *ββ-Methylethylglutaric acid*, m.p. 87°. *ββ-Methylpropylglutaric acid*, m.p. 92°. *ββ-Methylbutylglutaric acid*, m.p. 65°. *ββ-Diethylglutaric acid*, m.p. 108° (see C. 1901, I. 821).

αγγ-Trimethylglutaric acid, $CO_2H_2CH(CH_3)CH_2C(CH_3)_2CO_2H$, m.p. 97° (*cf.* Tetramethylsuccinic acid); *anhydride*, m.p. 96°, b.p. 262° (Ann. **292**, 220, C. 1906, II. 422). *αββ-Trimethylglutaric acid*, m.p. 88°, is obtained from camphoric acid (Vol. II), and α-cyano-αββ-trimethylglutaric ester; *anhydride*, m.p. 82° (C. 1899, I. 522); α-cyano-αββγ-tetramethylglutaric ester, produced by methylating α-cyano-α′ββ-trimethylglutaric ester, yields the *αββγ-tetramethyl-glutaric acids*, $CO_2H{\cdot}CH(CH_2)C(CH_3)_2CH(CH_3)CO_2H$, m.p. 140° and 90° (C. 1900, II. 466).

ααγγ-Tetramethylglutaric acid, $CH_2[C(CH_3)_2COOH]_2$, m.p. 186°, is produced from β-hydroxytetramethylglutaric acid by HI (C. 1900, II. 529).

Derivatives of Adipic Acid and Higher Dicarboxylic Acids

Adipic acid, $COOH{\cdot}[CH_2]_4{\cdot}COOH$, and its alkyl derivatives are volatile under diminished pressure without decomposition. (1) These acids, together with the higher homologues, are characterized by the formation of cyclic ketones when their calcium salts are heated (*Wislicenus*, Ann. **275**, 309). In the case of the higher acids, the use of the thorium salts yields better results. In many cases, small yields of cyclic diketones accompany the monoketones in this reaction (*Ruzicka* and others, many papers in Helv. Chim. Acta, **9**, and later volumes).


Adipic acid. *cyclo*Pentanone.
Pimelic acid. *cyclo*Hexanone.

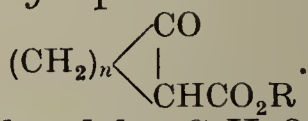
or in general,

$$(CH_2)_n{<}\begin{matrix}COOH\\COOH\end{matrix} \longrightarrow (CH_2)_n{>}CO$$

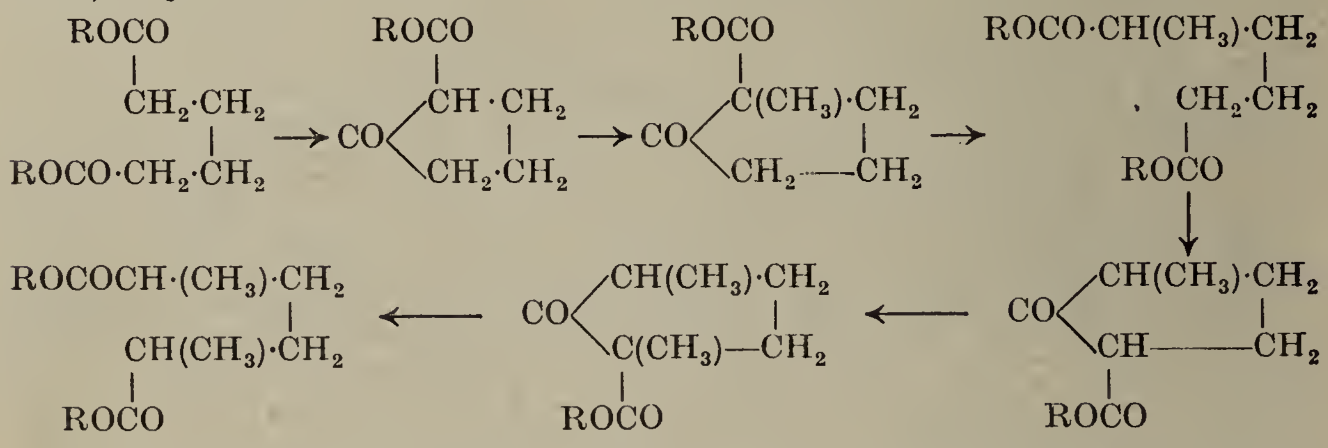
and

$$2(CH_2)_n{<}\begin{matrix}COOH\\COOH\end{matrix} \longrightarrow (CH_2)_n{<}\begin{matrix}CO\\CO\end{matrix}{>}(CH_2)_n.$$

The yield of many of these higher ketones is very small. *cyclo*Hexanone, obtained from pimelic acid, is obtained in 70% yield from the thorium salt, but the yield of *cyclo*decanone from the acid $(CH_2)_9(COOH)_2$ is only 0·1–0·2% of theory.

(2) Cyclic condensation can also be brought about by the action of sodium or sodium amide on the esters of adipic, pimelic acid, and, to a lesser extent, suberic acid ; β-keto-*cyclo*paraffin carboxylic esters are formed having the general formula  $(CH_2)_n{<}\begin{matrix}CO\\|\\CHCO_2R\end{matrix}$. Like acetoacetic ester, the CH-group can be alkylated by C_2H_5ONa and alkyl iodides, but when boiled with alcoholic sodium alcoholate the ring becomes broken, re-forming the dicarboxylic esters.

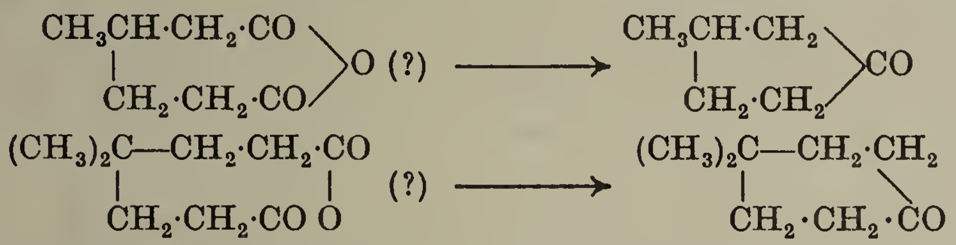
These reactions provide a method for alkylating adipic and pimelic acids in the α-position (Ann. **317**, 27 ; *cf.* C. 1905, II. **31** : 1908, I. 1169), *e.g.*—



(3) Adipic acid and the higher normal paraffin dicarboxylic acids, like succinic acid, tend to form anhydrides when boiled with acetyl

chloride or acetic anhydride. The resulting bodies probably do not consist of single molecules, but are multiples of them (Ber. **27**, R. 1105: C. 1896, II. 1091: 1907, I. 964) (*cf.* also the anhydrides of dialkylmalonic acids, p. 546).

The anhydrides obtained from adipic and pimelic acids and their alkyl substitution products by boiling with acetic anhydride, decompose when distilled into CO_2 and cyclic ketones (C. 1907, II. 685):



Adipic acid [hexane diacid], $CO_2H\cdot[CH_2]_4CO_2H$, m.p. 148°, b.p. 205·5°/10 mm., was first obtained by the oxidation of fats (*adeps* = fat) by nitric acid. It can also be formed by the oxidation of *cyclo*hexane, and most readily by oxidation of *cyclo*hexanone or *cyclo*hexanol, the products of reduction of phenol (Vol. II) by means of alkaline potassium permanganate (Ber. **39**, 2202: **41**, 575). It can be prepared (1) by reduction of hydromuconic acid (p. 577); (2) synthetically, from β-iodopropionic acid and silver at 130–140°, or copper at 160° (Ber. **28**, R. 466); (3) from ethyl potassium succinate, by electrolysis (Ann. **261**, 177); (4) from ethylene dimalonic acid or butane tetracarboxylic acid by loss of CO_2; (5) by hydrolysis and splitting of γ-cyanopropyl malonic ester or of tetramethylene dicyanide (C. 1901, I. 218, 610: II. 807).

The action of sodium converts adipic ester into β-*cyclo*pentanone monocarboxylic acid ester. Distillation of the calcium salt or anhydride results in the production of *cyclo*pentanone (Vol. II). *Amide*, m.p. 222° (Ber. **32**, 1772). *Adipic dinitrile, tetramethylene dicyanide*, m.p. 1°, b.p. 295°, is formed from tetramethylene bromide or iodide and KNC (C. 1901, I. 610: II. 807).

Alkyladipic acids.—α-*Methyladipic acid*, m.p. 64°. α-*Ethyladipic acid* is a liquid. β-*Methyladipic acid*, m.p. 89°, b.p. 211°/14 mm. It results from the oxidation of pulegone and menthone (Ann. **292**, 148); *ethyl ester*, b.p. 138°/15 mm. $[\alpha]_D + 2\cdot24°$. Condensation of the ester (see above) to methyl *cyclo*pentanone carboxylic ester is accompanied by a great increase in the optical rotation to $[\alpha]_D + 78\cdot24°$ (C. 1905, II. 31). α-iso*Propyladipic acid*, m.p. 67°, b.p. 222°/12 mm. (C. 1908, I. 1169, 1616).

Dialkyladipic acids are obtained (1) from *cyclo*pentanone carboxylic esters, by alkylation and breaking of the ring (see p. 560); (2) from ethylene bis-alkyl malonic esters; (3) from lactones or the bromo-fatty acids corresponding with them, by the action of KNC or sodium malonic ester or sodium cyanoacetic ester (*cf.* p. 534) (C. 1907, II. 897: 1908, I. 1616); (4) by oxidation of hydro-aromatic ketones (Vol. II). αδ-*Dimethyladipic acid*, two modifications, m.pp. 143° and 76°; dinitriles are produced from the two βε-dibromohexanes (p. 373), by KCN (Ber. **34**, 807). αα-*Dimethyladipic acid*, m.p. 90°. ββ-*Dimethyladipic acid*, m.p. 87° (C. 1905, I. 26: 1907, I. 239: 1908, I. 1616). αγ-*Dimethyladipic acid*, m.p. 80°. γ-*Methyl*-β-*ethyladipic acid*, m.p. 98°. αδ-*Methyl*iso*propyladipic acid*, m.p. 111°, etc.

Normal **pimelic acid** [heptane diacid], $CO_2H[CH_2]_5CO_2H$, m.p. 105° (Ann. **292**, 150), was first prepared by oxidizing suberone; and from salicylic acid by the action of sodium in amyl alcohol solution; *cyclo*hexanone carboxylic acid results as an intermediate product, and the ring is broken according to the formulæ on p. 560 (Ann. **286**, 259); by heating furonic acid, $C_7H_8O_5$, with HI; and in the oxidation of fats with nitric acid. It can be obtained synthetically from trimethylene bromide and malonic ester by heating pentamethylene tetracarboxylic acid, which is the first product of the reaction (Ber. **26**, 709). It may be conveniently prepared from the *dinitrile, pentamethylene dicyanide*, b.p. 172°/12 mm. This is obtained from crude dichloropentane (pp. 371, 373), and KCN (Ber. **37**, 3588: C. 1904, II. 587). When its calcium salt is distilled *cyclo*hexanone is produced (p. 560).

Alkylpimelic acids: α-, β-, and *γ-methylpimelic acids*, m.p. 54°, 49°, and 56°. They are formed when the *o*-, *m*-, and *p*-cresotic acids (Vol. II), or better, their dibromo-derivatives, are reduced by amyl alcohol and sodium (Ann. **295**, 173). The α-acid may also be prepared from the corresponding tetracarboxylic acid (Ber. **29**, 729), and by acid decomposition of methyl *cyclo*hexanone carboxylic ester (p. 560).

αε-Dimethylpimelic acids, m.p. 81° and 76° (Ber. **28**, R. 465).

αβε-Trimethylpimelic acid, b.p. 214°/15 mm. (Ber. **28**, 2943).

ββ-Dimethylpimelic acid, m.p. 104°, and *αγγ-trimethylpimelic acid*, m.p. 55°, are prepared from the condensation products of δ-bromo-β-dimethylcaproic ester and sodium malonic ester and sodium methylmalonic acid respectively. The *anhydrides* of these acids yield on distillation dimethyl*cyclo*hexanone and trimethyl*cyclo*hexanone (p. 561) (C. 1906, I. 1819: 1907, I. 964).

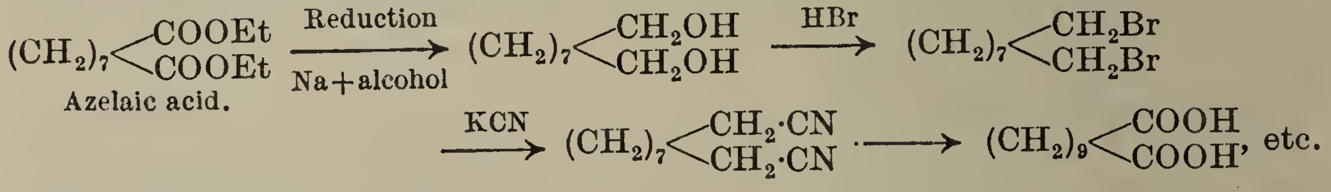
αε-Dibromopimelic acid, m.p. 141°; *diethyl ester*, b.p. 224°/28 mm., when acted on by sodium ethoxide yields *cyclo*pentene dicarboxylic acid (Vol. II).

Suberic acid [octane diacid], $CO_2H[CH_2]_6CO_2H$, m.p. 140°, is obtained by boiling cork (Ber. **26**, 3089), or fatty oils, with nitric acid (Ber. **26**, R. 814) (*suber* = cork). Its *ethyl ester*, b.p. 280–282°, has been synthesized by electrolysing potassium ethyl glutarate; it is also obtained by the action of magnesium and CO_2 on trimethylene bromide (p. 372) (Ber. **40**, 3039). Distillation of the calcium salt produces *suberone* (*cyclo*heptanone) (Ann. **275**, 356); *anhydride*, m.p. 62°; *diamide*, m.p. 216° (Ber. **31**, 2344); *dihydrazide*, m.p. 185°; *diazide*, m.p. 25° (see also αζ-hexamethylene diamine (p. 385) (J. pr. Chem. [2] **62**, 198). *βε-Tetramethylsuberic acid*, $[HOOC{\cdot}CH_2C(CH_3)_2{\cdot}CH_2]_2$, m.p. 165°, is produced from β-dimethylglutaric mono-ester, by electrolysis (C. 1906, II. 18).

Higher paraffin-dicarboxylic acids result, accompanied by oxalic, succinic and suberic acids, when fatty and oleic acids are oxidized by nitric acid.

The higher acetylene carboxylic acids (p. 352) usually decompose into the acids $C_nH_{2n-2}O_4$, when oxidized with fuming nitric acid. The mixture of acids that results is separated by fractional crystallization from ether; the higher members, being less soluble, separate out first (Ber. **14**, 560). Such acids have also been produced by the breaking-down of ketoximic acids through the action of concentrated sulphuric acid, *e.g.* sebacic acid from ketoxime stearic acid (p. 348).

The higher dicarboxylic acids can be built up from the lower, azelaic and sebacic acids, by the following series of reactions:



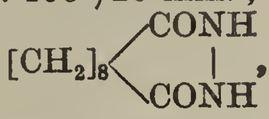
$$(CH_2)_7\Big\langle\begin{matrix}COOEt\\COOEt\end{matrix}\xrightarrow[\text{Na+alcohol}]{\text{Reduction}}(CH_2)_7\Big\langle\begin{matrix}CH_2OH\\CH_2OH\end{matrix}\xrightarrow{\text{HBr}}(CH_2)_7\Big\langle\begin{matrix}CH_2Br\\CH_2Br\end{matrix}$$

Azelaic acid.

$$\xrightarrow{\text{KCN}}(CH_2)_7\Big\langle\begin{matrix}CH_2{\cdot}CN\\CH_2{\cdot}CN\end{matrix}\longrightarrow(CH_2)_9\Big\langle\begin{matrix}COOH\\COOH\end{matrix},\ \text{etc.}$$

(Helv. Chim. Acta. **9**, 264).

Azelaic acid, *lepargylic acid*, [nonane diacid], $CO_2H[CH_2]_7CO_2H$, m.p. 106°, is obtained by the oxidation of oleic acid and castor oil by nitric acid or permanganate (Ber. **17**, 2214: C. 1900, I. 250). The name is derived from azotic acid = nitric acid, and elaidic acid, connected with oleic acid. It is synthetically prepared from pentamethylene bromide and sodium acetoacetic ester (Ber. **26**, 2249). When distilled with lime it yields azelaone (*cyclo*octanone); *ethyl ester*, b.p. 291° (Ann. **307**, 375); *anhydride*, m.p. 52°; *nitrile*, b.p. 195°/21 mm. (C. 1898, II. 848). *Azelaic dithiolic acid*, $COSH[CH_2]_7COSH$, m.p. 73°, is formed when azelaic diphenyl ester is treated with NaSH. Sodium converts it into a *disulphide*, $[CH_2]_7[CO_2]S_2$ (C. 1905, II. 217).

Sebacic acid [decane diacid], $CO_2H[CH_2]_8CO_2H$, m.p. 133°, is formed (1) by dry distillation of oleic acid; (2) by oxidation of stearic acid, spermaceti or castor oil by nitric acid; (3) from stearyl ketoxime; (4) from heptane tetracarboxylic acid (Ber. **27**, R. 413). *Anhydride*, m.p. 78°; *diethyl ester*, b.p. 196°/20 mm.; *dihydrazide*, m.p. 185°; *diazide*, m.p. 34°. sym.-*Sebacic hydrazide*,  $[CH_2]_8\left<\begin{matrix}CONH\\|\\CONH\end{matrix}\right.$, m.p. 142° (J. pr. Chem. [2] **62**, 216).

Nonane-αω-dicarboxylic acid, $[CH_2]_9(COOH)_2$, m.p. 110°, is obtained by the oxidation of ω-hydroxyundecoic acid (p. 429) by chromic acid, or synthetically from azelaic acid, as shown on p. 562.

Decanedicarboxylic acid $[CH_2]_{10}(COOH)_2$, m.p. 127°, is prepared from ω-bromoundecoic acid and KNC; also synthetically by electrolysis of pimelic mono-ester (Ber. **34**, 900: C. 1901, II. 1046).

Brassylic acid $[CH_2]_{11}(CO_2H)_2$, m.p. 114°, is obtained by oxidation of behenolic acid and erucic acid (Ber. **26**, 639, R. 705, 811). It is synthetically prepared by condensing ω-bromoundecoic ester and sodium malonic ester in alcohol, and subsequently hydrolysing and decomposing the condensation product. On the simultaneous formation of an isomeric acid (possibly α-methyldecanedicarboxylic acid), m.p. 82°, see Ber. **34**, 893 (*cf.* C. 1901, II. 1046).

Melting points of the *anilides* and *toluidides* of the more important dicarboxylic acids from C_3 to C_{13}, see J.C.S. **1927**, 2926.

Dodecanedicarboxylic acid, $[CH_2]_{12}(COOH)_2$, m.p. 126·5° (Helv. Chim. Acta, **9**, 271).

Tridecanedicarboxylic acid, $[CH_2]_{13}(COOH)_2$, m.p. 114° (Helv. Chim. Acta. **9**, 273).

Tetradecanedicarboxylic acid, $[CH_2]_{14}(COOH)_2$, m.p. 123° (Biochem. Z. **108**, 75).

Pentadecanedicarboxylic acid, $[CH_2]_{15}(COOH)_2$, m.p. 118° (Helv. Chim. Acta. **9**, 275), is formed by the decomposition of dihydrocivetone. *Rocellic acid,* $C_{17}H_{32}O_4$, m.p. 132°, occurs free in *Rocella tinctoria.*

Hexadecanedicarboxylic acid, $[CH_2]_{16}(COOH)_2$, m.p. 124°. Its thorium salt on distillation yields dihydrocivetone (Helv. Chim. Acta. **9**, 262, 276).

Heptadecanedicarboxylic acid, $[CH_2]_{17}(COOH)_2$, m.p. 119°.

Eicosanedicarboxylic acid, $[CH_2]_{20}(COOH)_2$, m.p. 123°: obtained by electrolysis of potassium ethyl decanedicarboxylate (Proc. Roy. Soc. Edin. **46**, 71).

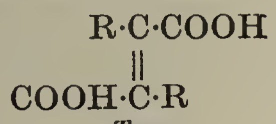
Tetracosanedicarboxylic acid, $C_{26}H_{50}O_4$, m.p. 123·5°.

Octacosanedicarboxylic acid, m.p. 123·5° (Proc. Roy. Soc. Edin. **46**, 71).

Higher methyl-substituted dicarboxylic acids, see Helv. Chim. Acta. **10**, 680, 691.

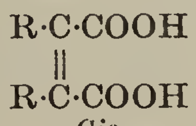
B. OLEFINEDICARBOXYLIC ACIDS, $C_nH_{2n-4}O_4$

The olefinedicarboxylic acids bear the same relation to the saturated dicarboxylic acids as the acrylic acid series to the fatty acids. In acids which have the two carboxyl groups attached to different carbon atoms, the acids are known in two stereoisomeric *cis-* and *trans*-forms, which show considerable differences from each other in their tendency to anhydride formation, and in the products they yield on oxidation at the ethylene linkage.



$$\begin{matrix}R\cdot C\cdot COOH\\ \|\\ COOH\cdot C\cdot R\end{matrix}$$

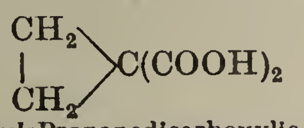
Trans.



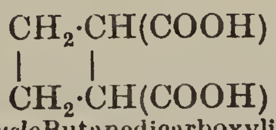
$$\begin{matrix}R\cdot C\cdot COOH\\ \|\\ R\cdot C\cdot COOH\end{matrix}$$

Cis.

These acids are isomeric with the *cyclo*paraffindicarboxylic acids containing the same number of carbon atoms, *e.g.*:



*cyclo*Propanedicarboxylic acid.



*cyclo*Butanedicarboxylic acid.

(*a*) Malonic Acid Derivatives

Methylenemalonic ester, $CH_2{=}C(CO_2C_2H_5)_2$, is produced together with β-ethoxymethylmalonic ester, $EtO{\cdot}CH_2{\cdot}CH(CO_2Et)_2$, when 1 molecule of methylene iodide and 2 molecules of sodium ethoxide act on 1 molecule of malonic ester (Ber. **23**, R. 194 : **22**, 3294 : Ann. **273**, 43). Under diminished pressure it distils as a mobile, badly-smelling oil. If allowed to stand, it soon changes into a white, solid mass, $(C_8H_{12}O_4)_2$ (C. 1898, II. 1169). The liquid ester unites with bromine. (See also β-Hydroxy*iso*succinic acid, p. 605.)

Ethylidenemalonic ester, $CH_3CH : C(CO_2C_2H_5)$, b.p. 116°/17 mm., is formed when acetaldehyde is condensed with malonic ester by acetic anhydride (Ann. **218**, 145). Malonic ester combines with it to form ethylidenedimalonic ester. Hydrolysis with barium hydroxide solution converts it into a hydroxy-carboxylic acid, $C_3H_5(OH)(CO_2H)_2$. *Trichloroethylidenemalonic ester*, $CCl_3CH : C(CO_2C_2H_5)_2$, b.p. 160°/23 mm., results when chloral and malonic ester are condensed by acetic anhydride (Ann. **218**, 145).

iso*Propylidenemalonic acid*, $(CH_3)_2C : C(CO_2H_2)$, m.p. 170° ; *ethyl ester*, b.p. 176°/120 mm., is formed from malonic ester and acetone by the action of acetic anhydride (Ber. **28**, 785, 1122, *cf.* Ber. **34**, 1955).

Cyanoacetic ester, reacting with aldehydes in the presence of sodium ethoxide, gives rise to olefine nitrile esters, such as *ethylidene cyanoacetic ester*, $CH_3CH : C(CN)CO_2R$ (C. 1901, I. 1271 : *cf.* C. 1898, I. 664). Cyanoacetic ester condensed with acetone by diethylamine, is converted into iso*propylidenecyanoacetic ester*, $(CH_3)_2C : C(CN)CO_2C_2H_5$, m.p. 28° (Ber. **33**, 3530 : C. 1905, II. 726).

Allylmalonic acid, $CH_2 : CH{\cdot}CH_2CH(CO_2H)_2$, m.p. 103°, is obtained from malonic ester by means of allyl iodide. It crystallizes in prisms (Ann. **216**, 52). Compare γ-Valerolactone, p. 427, and Carbovalerolactonic acid, p. 614. See Ber. **29**, 1856, and C. 1905, II. 660, for *ethylallylmalonic acid* and its homologues.

(*b*) Unsaturated Dicarboxylic Acids, in which the Carboxyl Groups are attached to two Carbon Atoms

Formation.—They can be obtained, like the acrylic acids, from the saturated dicarboxylic acids by the withdrawal of two hydrogen atoms. This is effected (1) by acting on the monobromo-derivatives with alkalis :

$$\underset{\text{Bromosuccinic acid.}}{C_2H_3Br(CO_2H)_2} \xrightarrow{-\text{HBr}} \underset{\text{Fumaric acid.}}{C_2H_2(CO_2H)_2} ;$$

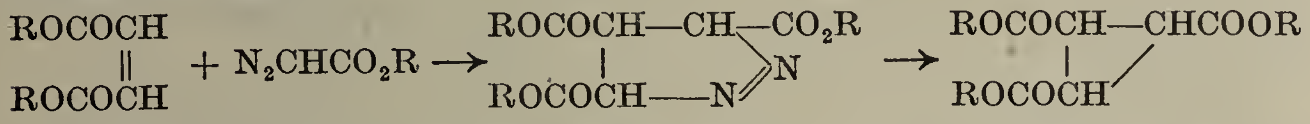
(2) by allowing potassium iodide to act on the dibromo-derivatives (p. 555). Thus, fumaric acid is formed from both dibromo- and *iso*dibromo-succinic acids :

$$C_2H_2Br_2(CO_2H)_2 + 2KI = C_2H_2(CO_2H)_2 + 2KBr + I_2 ;$$

and mesaconic acid, $C_3H_4(CO_2H)_2$, from citra- and mesa-dibromopyrotartaric acids, $C_3H_4Br_2(CO_2H)_2$. (3) From the hydroxydicarboxylic acids by the elimination of water (p. 604).

Behaviour.—The acids of this series show the same tendency to addition reactions as was observed with the unsaturated monocarboxylic acids. Thus (1) hydrogen causes them to revert to saturated dicarboxylic acids ; (2) halogen acids (particularly HBr) and (3) halogens convert them into haloid-saturated dicarboxylic acids. (4) When heated with potassium hydroxide an addition of hydrogen sometimes occurs with the production of monohydroxy-saturated dicarboxylic acids ; other acids are molecularly rearranged (Ber. **26**, 2082). Such rearrangement among isomers has been induced by boiling water or acids (*cf.* fumaric and maleic acids, mesaconic, citraconic and itaconic acids). (5) Potassium permanganate oxidizes some of the unsaturated dicarboxylic acids to dihydroxy-dicarboxylic acids of the paraffin series. (6) Amino- and substituted amino-dicarboxylic acids of the saturated series have been obtained by the addition of ammonia, aniline and other bases.

(7) The acids of this series combine with diazomethane or diazoacetic acid, yielding pyrazoline derivatives (Ann. **273**, 214 : Ber. **27**, 868), which pass into trimethylene derivatives by the elimination of nitrogen (p. 459) :



Fumaric and maleic acids, the first members of this series, are the most important acids of their class.

Fumaric and Maleic Acids

Fumaric acid, $C_2H_2(CO_2H)_2$, occurs free in many plants, in Iceland moss, in *Fumaria officinalis,* and in some fungi.

It is formed (1) when inactive and active malic acid are heated (water and maleic anhydride are also produced) (Ber. **12**, 2281 : **18**, 676), and by boiling malic acid with sodium hydroxide solution (Ber. **33, 1453**) ; (2) by boiling the aqueous solutions of monochloro- and monobromo-succinic acids ; (3) from dibromo- and *iso*dibromo-succinic acids and potassium iodide ; (4) synthetically from dichloro- or dibromoacetic acid and silver malonate ; also from glyoxylic acid and malonic acid by heating them with pyridine (Ber. **34**, 53) ; (5) from maleic acid (see the conversion of fumaric and maleic acids into each other, p. 567) ; (6) by boiling with water bromosuccinyl bromide, the reaction product of phosphorus and bromine on succinic acid (Ber. **23**, 3757).

Properties.—It is almost insoluble in cold water, but crystallizes from hot water in small, white needles. It sublimes at 200°, and at higher temperatures decomposes, forming maleic anhydride and water.

Salts.—The *silver salt,* $C_4H_2O_4Ag_2$, is very insoluble ; it is fairly stable under the influence of light ; *barium salt,* $C_4H_2O_4Ba + 3H_2O$, consists of prismatic crystals, which effloresce and when boiled with water change to $C_4H_2O_4Ba$—a salt that is practically insoluble in water.

Esters.—The fumaric esters are formed (1) from the silver salt and alkyl iodides ; (2) from fumaric acid, alcohols and hydrochloric acid ; (3) from the esters of monobromosuccinic acid by the action of pyridine or quinoline (C. 1905, I. 25) ; by the slow distillation of malic and acetyl malic esters (Ber. **22**, R. 813) ; (4) from maleic esters (see interchange between fumaric and maleic acids, p. 567) ; (5) by heating diazoacetic esters (Ber. **29**, 763).

Methyl ester, $C_2H_2(CO_2CH_3)_2$, m.p. 102°, b.p. 192° ; *ethyl ester,* b.p. 218° (Ber. **12**, 2283). Bromine unites with fumaric esters to form dibromosuccinic esters. Many other substances have the power of adding themselves to them, *e.g.* sodium acetoacetic ester, sodium malonic ester (Ber. **24**, 309, 2887, R. 636), sodium cyanoacetic ester (Ber. **25**, R. 579), diazoacetic ester (above) phenyl azoimide, etc.

Fumaryl chloride, COCl·CH : CH·COCl, b.p. 160°, is produced when PCl_5 or phthalyl chloride (Vol. II) acts on fumaric acid (Ber. **18**, 1947 : C. 1906, II. 19). Bromine converts it into dibromosuccinyl chloride (Ann. Suppl. **2**, 86) ; and with sodium peroxide it yields *fumaric peroxide,* $C_4H_2O_4$, a white powder, exploding at 80° (Ber. **29**, 1726).

Fumaramic acid, $CONH_2·CH : CH·CO_2H$, m.p. 217°, is formed when asparagine is acted on by methyl iodide and potassium hydroxide (Ann. **259**, 137).

Fumaramide, $CONH_2CH : CH\cdot CONH_2$, m.p. 266° (Ber. **25**, 643). P_2O_5 converts it into fumaronitrile (J.A.C.S., **40**, 970).

Fumarhydrazide, $NH_2NH\cdot CO\cdot CH : CH\cdot CO\cdot NHNH_2$, m.p. 220° (decomp.). *Fumarazide,* $N_3CO\cdot CH : CH\cdot CON_3$, is crystalline. It explodes easily, and when boiled with alcohol yields acetylenediurethane, ROCONHCH : CHNHCOOR (Ber. **29**, R. 231).

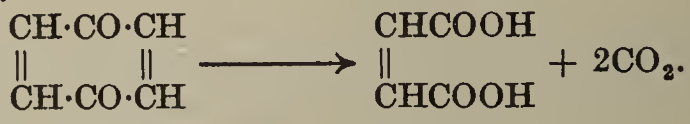
Fumaranilic acid, $C_6H_5NH\cdot COCH : CH\cdot CO_2H$, m.p. 231°, is formed from the corresponding chloride and water. *Fumaranilic chloride,* $C_6H_5NH\cdot CO\cdot CH : CH\cdot COCl$, m.p. 120°, crystallizes from ether in transparent, strongly refracting, sulphur-yellow coloured prismatic needles or plates. It is produced when aniline acts on fumaryl chloride in excess. *Fumardianilide,* $C_6H_5NHCOCH : CHCONH\cdot C_6H_5$, m.p. 234° (decomp.) (Ann. **239**, 144 : C. 1906, II. 19).

Maleic acid, $C_4H_4O_4$, m.p. 135°, b.p. 160°, with decomposition into maleic anhydride and water. Its anhydride is formed as mentioned under fumaric acid : (1) By the rapid heating of malic acid. (2) In the slow distillation of monochloro- and monobromosuccinic acid, as well as acetylmalic anhydride at the ordinary pressure. (3) By the action of PCl_5 on malic acid (Ann. **280**, 216).

(4) Maleic acid is formed synthetically, in small amount, when silver or sodium acts on dichloroacetic acid and dichloroacetic ester.

(5) Maleic acid is obtained on decomposing trichlorophenomalic acid or β-trichloroacetylacrylic acid (p. 481) with barium hydroxide solution. Chloroform is produced at the same time.

(6) From quinone (Vol. II) by oxidation with silver peroxide (Ber. **39**, 3715) :

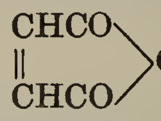


$$\begin{array}{l}CH\cdot CO\cdot CH\\ \| \qquad\quad \|\\ CH\cdot CO\cdot CH\end{array} \xrightarrow{\qquad} \begin{array}{l}CHCOOH\\ \|\\ CHCOOH\end{array} + 2CO_2.$$

(7) From fumaric acid (see p. 567).

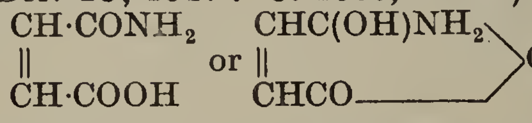
Properties.—Maleic acid crystallizes in large prisms or plates, is very easily soluble in cold water, and possesses a peculiar, disagreeable taste.

Salts.—$C_4H_2O_4Ag_2$ is a finely divided precipitate. It gradually changes to large crystals. $C_4H_2O_4Ba + H_2O$ is soluble in hot water, and crystallizes well. The *esters* result from the action of alkyl iodides on the silver salt. *Methyl ester,* $C_2H_2(CO_2\cdot CH_3)_2$, is a liquid, b.p. 205° ; *ethyl ester,* b.p. 225°. When heated with iodine they change for the most part into fumaric esters.



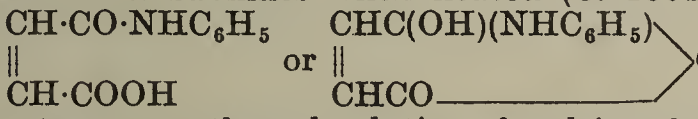
Maleic anhydride, $\left.\begin{array}{l}CHCO\\ \|\\ CHCO\end{array}\right\rangle O$, m.p. 53°, b.p. 202°, is produced (1) by distilling maleic or fumaric acid alone, or more readily (2) with acetyl chloride or P_2O_5 (Ber. **37**, 3722) ; (3) by the distillation of monochloro- and monobromosuccinic acids, and also of acetomalic anhydride (Ann. **254**, 155) ; (4) when PCl_5, P_2O_5 and $POCl_3$ act on fumaric acid (Ann. **268**, 255). It is purified by crystallization from chloroform (Ber. **12**, 2281 : **14**, 2546). It consists of needles or prisms, having a faintly penetrating odour. It regenerates maleic acid by union with water, and forms *iso*dibromosuccinic anhydride when heated with bromine (*cf.* Asparagine, p. 609).

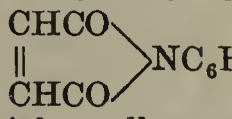
Maleic chloride (Ber. **18**, 1947 : C. 1906, II. 20).

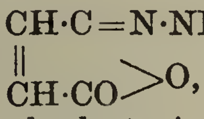
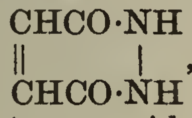


Maleinamic acid, $\begin{array}{l}CH\cdot CONH_2\\ \|\\ CH\cdot COOH\end{array}$ or $\left.\begin{array}{l}CHC(OH)NH_2\\ \|\\ CHCO\end{array}\right\rangle O$, m.p. 153°. Its ammonium salt results when ammonia acts on maleic anhydride. Aqueous potassium hydroxide converts the acid into maleic acid, whereas fumaric acid results when it is treated with alcoholic potassium hydroxide. *Maleinmethylamic acid,* m.p. 149° (Ber. **29**, R. 653).

Maleinimide, $C_2H_2(CO)_2NH$, m.p. 93°, is produced when pyrrole is oxidized by chromic acid mixture. It sublimes when heated (C. 1904, II. 305).

Maleinanilic acid, 
$\begin{array}{l}\text{CH·CO·NHC}_6\text{H}_5\\ \|\\ \text{CH·COOH}\end{array}$ or $\begin{array}{l}\text{CHC(OH)(NHC}_6\text{H}_5)\\ \|\\ \text{CHCO}\end{array}\!\!>\!\text{O}$, m.p. 187°, is formed when aniline acts on an ethereal solution of maleic anhydride. Heated under greatly reduced pressure it splits into maleic anhydride and aniline, which reunite in the receiver to maleinanilic acid. Alcoholic potassium hydroxide and barium hydroxide solution convert it into fumaric acid (Ann. **259**, 137).

Maleinanil, 
$\begin{array}{l}\text{CHCO}\\ \|\\ \text{CHCO}\end{array}\!\!>\!\text{NC}_6\text{H}_5$, m.p. 91°, results upon heating aniline malate, in the form of bright yellow needles. It combines readily with aniline, forming phenyl asparaginanil (Ann. **239**, 154). *Maleindianilide,* m.p. 175° (C. 1901, I. 171).

N-*Aminomaleinimide,* 
$\begin{array}{l}\text{CH·C=N·NH}_2\\ \|\\ \text{CH·CO}\end{array}\!\!>\!\text{O}$, m.p. 111°, is obtained from maleic anhydride and hydrazine hydrate in alcohol. When its solution is heated it changes to *malein hydrazide,* 
$\begin{array}{l}\text{CHCO·NH}\\ \|\qquad\quad\ |\\ \text{CHCO·NH}\end{array}$, consisting of white crystals, which do not melt at 250°. It is a strong acid.

Reactions of Fumaric and Maleic Acids

1. Acetylene is formed when the alkali salts of these acids are electrolysed (p. 109).
2. Sodium amalgam, or zinc, reduces them both to succinic acid.
3. When heated to 100° with sodium hydroxide both acids change to inactive malic acid (Ann. **269**, 76), whilst malic acid is changed into fumaric acid when boiled with sodium hydroxide solution (p. 605).
4. Fumaric and maleic esters react with sodium alcoholates to form alkylhydroxy-succinic acids (Ber. **18**, R. 536).
5. Bromine converts fumaric acid, its ester and chloride into dibromosuccinic acid, its ester and chloride, and maleic anhydride into *iso*dibromosuccinic anhydride (*cf.* J.A.C.S. **47**, 1067, 1402).
6. Potassium permanganate oxidizes fumaric acid to racemic acid and maleic acid to *meso*tartaric acid (Ber. **14**, 713 : see also J.A.C.S. **47**, 1412).

Conversion of Fumaric and Maleic Acids into each other

1. When fumaric acid is heated, or treated with PCl_5, $POCl_3$ and P_2O_5 (Ann. **268**, 255 : **273**, 31) it yields maleic anhydride.
2. Maleic acid changes to fumaric acid :

(*a*) When it is heated alone in a sealed tube to 200° (Ber. **27**, 1365).

(*b*) By the action of cold HCl, HBr, HI and other acids ; also SO_2 and H_2S (Ber. **24**, R. 823), N_2O_3 (Ber. **33**, 3241), as well as by the action of bromine in sunlight (Ber. **29**, R. 1080).

(*c*) On heating maleic ester with iodine fumaric esters result.

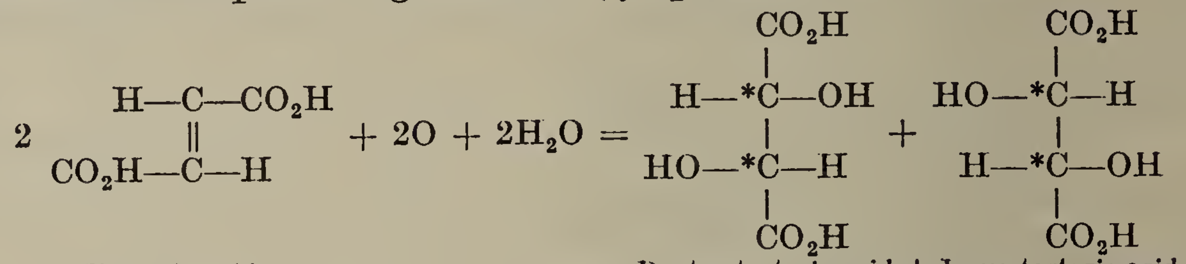
(*d*) Alcoholic potassium hydroxide changes maleinamic and maleinanilic acids to fumaric acid.

(For theoretical considerations of interconversion of maleic → fumaric acid, see J.A.C.S. **47**, 1067, 1402.)

The Isomerism of Fumaric and Maleic Acids

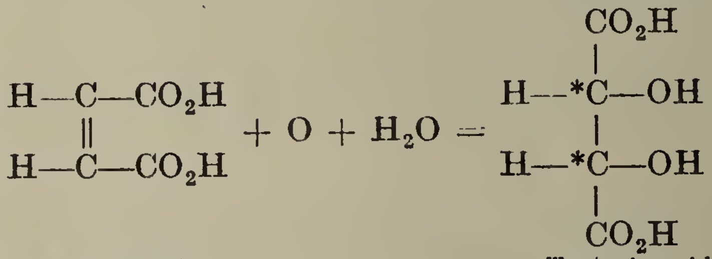
The view generally accepted as to the cause of the isomerism of these two acids was presented in the introduction, under the section relating to the geometrical isomerism of the ethylene derivatives (p. 41). In conformity with this representation we find in maleic acid, readily forming an anhydride, an atomic grouping which follows the *cis*- configuration, according to which the carboxyl groups are so closely arranged with reference to each other that the production of an anhydride follows without difficulty. Fumaric acid is not capable of forming an anhydride, hence it has the *trans*- or axial symmetrical structure.

These space-formulæ satisfactorily represent the intimate connection existing, as shown by Kekulé and Anschütz, between fumaric and racemic acids, and maleic and inactive tartaric acids. According to the van 't Hoff-Le Bel view of these four acids, the oxidation of fumaric to racemic acid by means of potassium permanganate and maleic to *meso*tartaric acid, may be shown by the following formulæ, which have a spacial significance (*cf.* p. 41):



$$2\ \begin{array}{c} H—C—CO_2H \\ \| \\ CO_2H—C—H \end{array} + 2O + 2H_2O = \begin{array}{c} CO_2H \\ | \\ H—{}^*C—OH \\ | \\ HO—{}^*C—H \\ | \\ CO_2H \end{array} + \begin{array}{c} CO_2H \\ | \\ HO—{}^*C—H \\ | \\ H—{}^*C—OH \\ | \\ CO_2H \end{array}$$

Fumaric acid. Dextro-tartaric acid + Lævo-tartaric acid = Racemic acid.

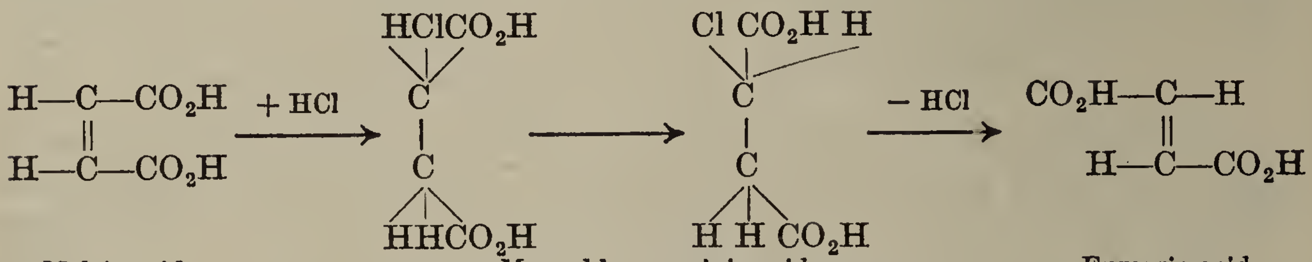


$$\begin{array}{c} H—C—CO_2H \\ \| \\ H—C—CO_2H \end{array} + O + H_2O = \begin{array}{c} CO_2H \\ | \\ H—{}^*C—OH \\ | \\ H—{}^*C—OH \\ | \\ CO_2H \end{array}$$

Maleic acid. *meso*Tartaric acid.

The oxidation of the two acids, based on stereochemical formulæ, is so represented that upon severing the double linkage in fumaric acid by the addition of hydroxyl groups an equal number of molecules of dextro- and lævo-tartaric acid results, whilst by the rupture of the double linkage in maleic acid only *meso*tartaric acid is formed.

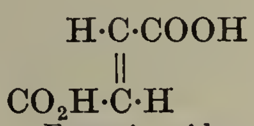
Cognizant of this view, J. Wislicenus has sought to explain the conversion of maleic into fumaric acid by hydrochloric acid in the following manner: In these two acids the two double-linked carbon atoms cannot rotate independently of each other, consequently not in opposite directions; but when the double union is removed by the addition of two univalent atoms, then free rotation at the single bond can occur. Accordingly, J. Wislicenus' explanation proceeds, in his own words, as follows: "On account of the extreme ease with which maleic acid, in contrast to fumaric acid, lends itself to the formation of addition products (Ber. **12**, 2282), it first absorbs the elements of the mineral acids (*e.g.*, HCl), and becomes converted into a substituted succinic acid, which, under the directing influence of the greater affinities, assumes the preferred configuration (in which similar groups are as far removed from each other as possible) by the rotation of the one system in opposition to the other, and then by the loss of HCl, under the influence partly of the water which is present and partly of the slight solubility of fumaric acid, the latter acid must result."



Maleic acid. Monochlorosuccinic acid previous to rotation. Monochlorosuccinic acid after rotation in the preferred position. Fumaric acid.

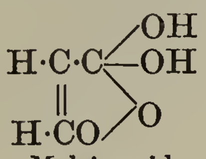
This explanation of Wislicenus is, however, not satisfactory, as the monochlorosuccinic acid postulated as an intermediate is known in the free condition, and under the above reaction conditions yields no fumaric acid (Anschütz, Ann. **254**, 168). Many other facts are not in agreement with the above explanation (*cf.* Ber. **20**, 3306 : **24**, R. 822 : **24**, 3620 : **25**, R. 418 : **26**, R. 177 : Ann. **259**, 1 : **280**, 226 : J. pr. Chem. [2] **75**, 105 : *cf.* Z. physik. Chem. **48**, 40).

Attempts have also been made to represent the isomerism of fumaric and maleic acids structurally, fumaric acid being represented as ethylenedicarboxylic acid (I), while maleic acid is represented as the γ-dihydroxylactone (II) :



$$\begin{matrix} H{\cdot}C{\cdot}COOH \\ \| \\ CO_2H{\cdot}C{\cdot}H \end{matrix}$$

Fumaric acid.
(I)



Malcic acid.
(II)

However, even this view, as yet, does not afford a satisfactory explanation of the reactions by which these acids are converted into each other. Consult Ann. **461**, 155, for the history of the isomerism of fumaric and maleic acids.

The various ideas as to the cause of the isomerism of fumaric and maleic acids are connected with the question as to the nature of the double linkage (p. 44).

Finally, attention may be directed to the difference in the heat of combustion of the acids. This would indicate that the energy present in the acids, in the form of atomic motion, is markedly different. " This fact suggests the possibility that the cause of the isomerism is not to be sought exclusively in the varying arrangement of the atoms, nor in their different spacial positions, but also in the varying magnitude of the motion of the atoms (or atom complexes)." " It is also possible to imagine a case in which the isomerism would only be influenced by the difference in energy content—a case in which there might be perfect similarity in linkage and also in the spacial arrangement of the atoms."

In addition to structural and spacial isomerism, there is the hypothesis of *energy* or *dynamical isomerism* (*Tanatar*, Ann. **273**, 54 : Ber. **11**, 1027 : **29**, 1300), to which this name is more applicable than to that to which attention has been drawn in connection with the *sym.*-dialkylsuccinic acids (p. 549). Klinger proposes the name " *alloergatia* " (from ergasia or ergatia) for that type of isomerism when molecules of the same weight and chemical construction contain unequal quantities of energy (Ber. **32**, 2194).

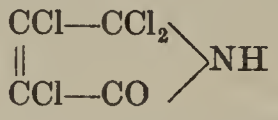
Halogen Derivatives of Fumaric and Maleic Acids

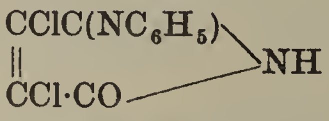
Monochlorofumaric acid, $C_4H_3ClO_4$, m.p. 192°, results (1) from tartaric acid and PCl_5 or PCl_3 ; (2) from the two dichlorosuccinic acids ; (3) from acetylenedicarboxylic acid and fuming hydrochloric acid. *Monochloromaleic acid*, m.p. 106° ; *anhydride*, m.pp. 0° and 34°, b.p. 197°/760 mm., b.p. 95°/25 mm., is produced when acetyl chloride acts on chlorofumaric acid, and when *iso*dichlorosuccinic anhydride is heated (Ann. **280**, 222).

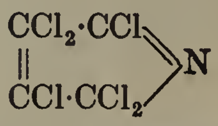
Monobromofumaric acid, $C_4H_3BrO_4$, m.p. 179°, is produced from acetylenedicarboxylic acid and HBr ; and from *iso*dibromosuccinic acid and boiling water. *Monobromomaleic acid*, m.p. 128°, is formed when dibromosuccinic acid—the addition product of bromine and fumaric acid—is boiled with water ; *ester*, b.p. 140°/12 mm., is prepared from dibromosuccinic ester and quinoline (C. 1905, I. 26) ; *anhydride*, b.p. 215°, is prepared by heating *iso*dibromosuccinic anhydride and dibromosuccinic acid, either alone or with acetic anhydride or acetyl chloride. The action of HBr is to produce bromofumaric acid and some dibromosuccinic acid.

Monoiodofumaric acid, m.p. 183° (Ber. **15**, 2697).

Dichloromaleic acid, $C_4Cl_2H_2O_4$, results when hexachloro*cyclo*hexenedione, $CO\Big\langle{CCl=CCl \atop CCl_2-CCl_2}\Big\rangle CO$, and perchloroacetylacrylic acid, $CCl_3CO{\cdot}CCl=CCl{\cdot}CO_2H$ (p. 481), are decomposed by sodium hydroxide (Ann. **267**, 20 : Ber. **25**, 2230). On the application of heat it passes into the *anhydride*, $C_2Cl_2(CO)_2O$, m.p. 120°. PCl_5 converts succinic chloride into two isomeric *dichloromaleic chlorides* (Ber. **18**, R. 184 : C. 1900, I. 404). Its *imide*, $C_2Cl_2(CO_2)_2NH$, m.p. 179°, is obtained when succinimide is heated in a current of chlorine. One molecule of PCl_5 changes the imide to *dichloromaleinimide chloride* (1), m.p. 148°, which is also formed from PCl_5 and succinimide. Aniline converts it into *dichloromaleinimide anil* (2), m.p. 152°. Two molecules of PCl_5 transform dichloromaleinimide into *pentachloropyrrole* (3), b.p. 90·5°/10 mm.:

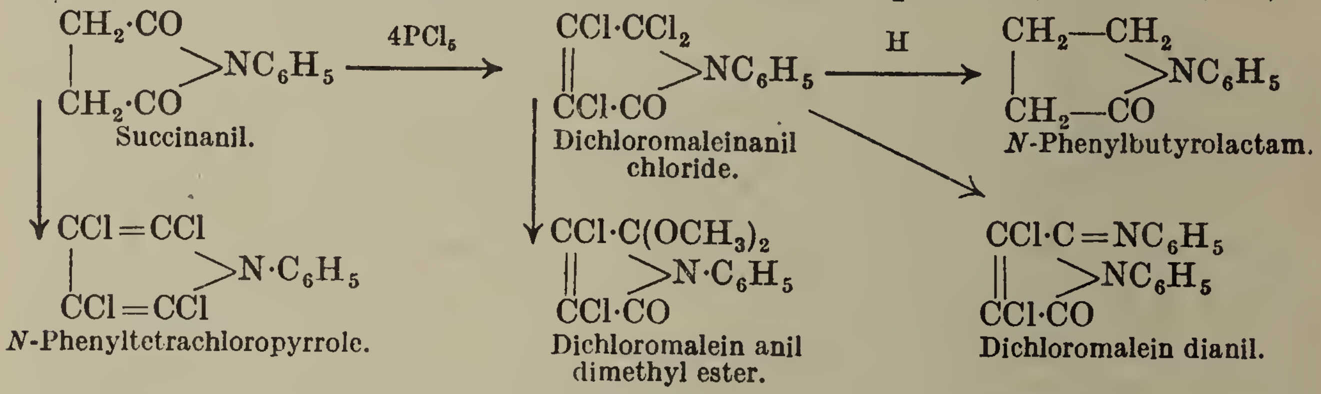
(1) 

(2) 

(3) 

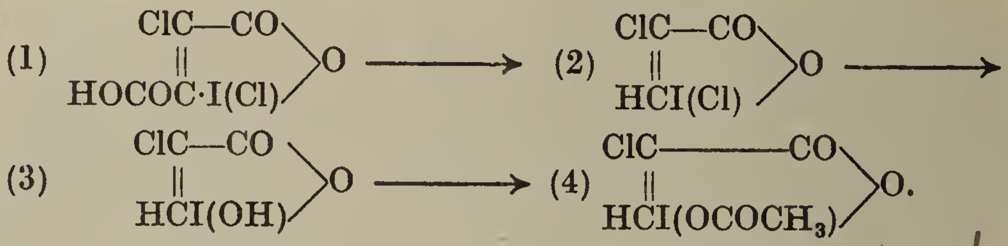
Dichloromalein anil, $C_2Cl_2(CO)_2NC_6H_5$, m.p. 203°, is formed when dichloromalein anil chloride is boiled with glacial acetic acid or water.

Dichloromalein anil chloride, m.p. 124°, b.p. 179°/11 mm., is produced, together with *tetrachloro-*N*-phenylpyrrole*, m.p. 93°, on treating succinanil with PCl_5. By reduction it yields δ-anilidobutyrolactam (see Succinimide, p. 552). Alcohols convert it into dialkyl esters: *dichloromalein anil dimethyl ester*, m.p. 110°; whilst with aniline it yields *dichloromalein dianil*, m.p. 187° (Ann. **295**, 27):



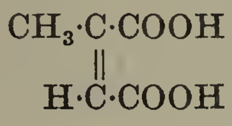
Dibromomaleic acid, $C_2Br_2(CO_2H)_2$, m.p. 120–125°, is obtained by acting on succinic acid with Br (C. 1900, I. 404), or by the oxidation of mucobromic acid with bromine water, silver oxide or nitric acid. It is very readily soluble, and readily forms the *anhydride*, $C_2Br_2(CO)_2O$, m.p. 115° (Ber. **13**, 736). *Chlorobromomaleic acid*, see Ber. **29**, R. 186.

Dibromofumaric acid, m.p. 219–222°, and *di-iodofumaric acid* (decomp. at 192°), are addition products of bromine and iodine with acetylenedicarboxylic acid (Ber. **12**, 2213 : **24**, 4118). *Chloriodofumaric acid*, m.p. 227° (decomp.), unites with chlorine to form an *iodosochloride* (1) (*cf.* p. 164). It reacts with alcohol, losing CO_2 and forms chloroacrylic acid iodosochloride (2); which, with hot water, yields *iodosochloroacrylic acid* (3); and finally this, with glacial acetic acid to form iodosochloroacrylic acid acetate (4) (Ber. **38**, 2842):

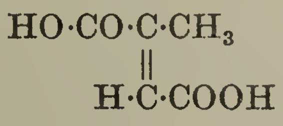


Acids, $C_3H_4(COOH)_2$

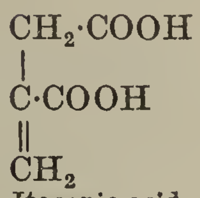
In addition to ethylidenemalonic acid already described (p. 564) and three *cyclo*propanedicarboxylic acids, there are four unsaturated dicarboxylic acids of this formula, *itaconic*, *citraconic*, *mesaconic* and *glutaconic* acids. The first three of these acids are closely related. Mesaconic and citraconic acids are respectively the *trans-* and *cis-* acids, methylfumaric and methylmaleic acids, while itaconic acid, methylenesuccinic acid, though structurally different, is closely related to them, and the double bond between the α- and β-carbon atoms of the first two acids can shift under certain conditions to the βγ-position of itaconic acid and vice versa. Citraconic anhydride is more readily obtained from citraconic acid than maleic anhydride from maleic acid and combines less readily with water than the latter: heating of citraconic acid under reduced pressure at 100° is sufficient to bring about anhydride formation. The action of acetyl chloride on mesaconic acid also yields citraconic anhydride more readily than fumaric acid yields maleic anhydride :


$$\begin{array}{l} CH_3{\cdot}C{\cdot}COOH \\ \quad\;\, \| \\ \quad H{\cdot}C{\cdot}COOH \end{array}$$

Citraconic acid.

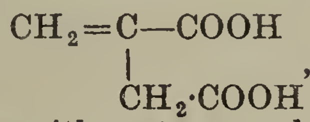

$$\begin{array}{l} HO{\cdot}CO{\cdot}C{\cdot}CH_3 \\ \qquad\qquad \| \\ \qquad\quad H{\cdot}C{\cdot}COOH \end{array}$$

Mesaconic acid.

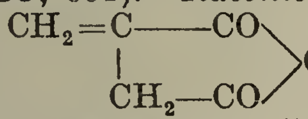

$$\begin{array}{l} CH_2{\cdot}COOH \\ | \\ C{\cdot}COOH \\ \| \\ CH_2 \end{array}$$

Itaconic acid.

Glutaconic acid is structurally different from the above, and has the formula $COOH{\cdot}CH:CH{\cdot}CH_2{\cdot}COOH$ (see p. 575).

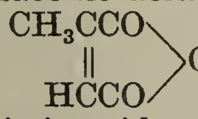
Itaconic acid, *methylenesuccinic acid*,  $\begin{array}{l} CH_2{=}C{-}COOH \\ \quad\;\; | \\ CH_2{\cdot}COOH \end{array}$, m.p. 161°, is produced from its anhydride by combination with water ; or by heating citraconic anhydride with 3 to 4 parts of water at 150°, whereby the citraconic anhydride is first transformed into itaconic anhydride which is then converted into the acid. It is not volatile in steam. Hydrogen converts it into pyrotartaric acid, and permanganate into hydroxyparaconic acid (*q.v.*) (Ann. **305**, 41). When electrolysed it yields allene, $CH_2{=}C{=}CH_2$ (p. 114). When boiled with aniline it forms *pseudo*-itaconanilic acid, the lactam of γ-anilinopyrotartaric acid (p. 611) (Ann. **254**, 129). On the addition of HBr and Br_2, see pp. 554, 555.

Itaconic dimethyl ester, m.p. 38°, b.p. 108°/11 mm., when not quite pure, polymerizes into a glassy variety possessing a strong refractive index (Ber. **14**, 2787 : Ann. **248**, 203 : Ber. **38**, 691). *Itaconic mono-esters* (Ber. **30**, 2649).

Itaconic anhydride,  $\begin{array}{l} CH_2{=}C{-}CO \\ \quad\;\; | \\ \quad CH_2{-}CO \end{array}\!\!\Big>O$, m.p. 68°, b.p. 146°/30 mm. Its name is formed by interchanging the syllables of aconitic acid. Itaconic anhydride is obtained from the hydrate (Ber. **13**, 1539), and from the silver salt by means of acetyl chloride (Ber. **13**, 1844). It has been found in the distillate obtained when citric acid is heated (Ber. **13**, 1542), and is probably produced by the decomposition of the aconitic acid which is first formed. It crystallizes from chloroform. When distilled at ordinary pressures it passes into citraconic anhydride, which unites with water far less readily than itaconic anhydride.

Itaconanilic acid, m.p. 151·5 (Ann. **254**, 140).

Citraconic acid, *methylmaleic acid*, m.p. 91°, is formed when its anhydride takes up water. The acid itself is soluble in water. Its volatility in steam is due to its decomposition below 100° into water and the anhydride which volatilizes. It resembles mesaconic acid in its behaviour towards KMnO4 (below).

Citraconic anhydride,  $\begin{array}{l} CH_3CCO \\ \quad\;\; \| \\ \quad HCCO \end{array}\!\!\Big>O$, m.p. 7°, b.p. 213°, is found among the distillation products of citric acid, probably through the transformation of the first-formed itaconic anhydride. It is formed when citraconic acid or mesaconic acid is heated alone ; and when treated with acetyl chloride. Prolonged heating at about 200° changes it partly into xeronic acid or diethylmaleic anhydride (p. 574). *Bromocitraconic anhydride*, m.p. 99° (Ber. **27**, 1855). *Citraconeins* are pigments prepared by the condensation of citraconic anhydride and phenols by the action of $SnCl_4$ (see Q.J. Indian Chem. Soc. **4**, 253).

Hydrogen converts citraconic and mesaconic acids (below) into pyrotartaric acid. Addition products with halogens and halogen acids have been examined already as substitution products of pyrotartaric acid (p. 557). Either acid, when electrolysed, yields *allylene*, $CH_3C{\equiv}CH$ (p. 112).

Citraconanilic acid, m.p. 153° (Ann. **254**, 135).

Citraconanil, m.p. 98° (Ber. **23**, 2979 : **24**, 314).

Mesaconic acid, *methylfumaric acid*, *hydroxytetrinic acid*, $C_3H_4(CO_2H)_2$, m.p. 202°, is formed when citraconic or itaconic acid is heated with a small quantity of water at 200° ; by the action of sunlight on an ether-chloroform solution of citraconic acid, containing a trace of bromine ; by heating citraconic acid with dilute nitric acid, concentrated halogen acids, or concentrated sodium hydroxide solution (Ann. **269**, 182 : Ber. **27**, R. 412) (*cf.* α- and β-Methylmalic acid, p. 611); and from dibromomethylacetoacetic acid (p. 476). It is soluble with difficulty in water, and is non-volatile in steam. $KMnO_4$ oxidizes it to pyroracemic and oxalic acids (Ann. **305**, 407); *barium salt*, $C_5H_4O_4Ba + 4H_2O$; *dimethyl ester*, b.p. 203°; *diethyl ester*, b.p. 229°.

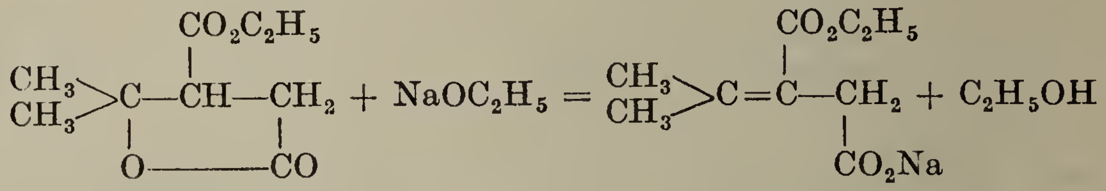
The relation between the results of partial hydrolysis and of esterification of the mesaconic acids have been investigated in detail. Hydrolysis of the di-alkyl ester yields *α-mesaconic monomethyl ester*, m.p. 84°, and *monoethyl ester*, m.p. 68°, $HOCO{\cdot}CH:C(CH_3)COOR$; whilst partial esterification yields a mixture of α-mesaconic acid esters and *β-mesaconic monomethyl ester*, m.p. 52°, and *monoethyl ester*, m.p. 67°, $HOCO{\cdot}C(CH_3):CHCOOR$. The structure of the latter bodies is demonstrated by their being prepared in a state of purity when γ-dibromo-α-methylacetoacetic ester (p. 476) is boiled with water and barium carbonate.

Mesaconyl chloride, $ClOC{\cdot}C(CH_3):CHCOCl$, b.p. 65°/14 mm., reacts with two molecules of aniline and forms *α-mesaconanilide acid chloride*, $ClOC{\cdot}C(CH_3):CHCONHC_6H_5$ (Ann. **353**, 139).

Bromomesaconic acid, m.p. 220° (Ber. **27**, 1851, 2130).

The *homologues of itaconic, citraconic, mesaconic and aticonic acids* have become known mainly by the painstaking investigations of R. Fittig and his co-workers (Ann. **304**, 117: **305**, 1).

The parent substances from which these acids are formed are the alkylparaconic acids (p. 612), which are prepared by condensation of aldehydes with succinic acid or pyrotartaric acid by means of acetic anhydride. On distillation they yield unsaturated monobasic acids, and anhydrides of two acids of the itaconic and citraconic series isomeric with the particular paraconic acid employed. If the alkylparaconic esters are warmed with sodium alcoholate in alcoholic solution they are converted into the sodium salts of the corresponding itaconic mono-esters, from which the acids themselves are obtained by hydrolysis (Ann. **255**, 56: **256**, 50). Thus, terebic acid and sodium ethoxide produce teraconic acid; and similarly γ-dimethylparaconic acid yields γ-dimethylitaconic acid:



$$\underset{O\text{———————}CO}{{}^{CH_3}_{CH_3}{>}\underset{|}{C}—\overset{CO_2C_2H_5}{\overset{|}{C}H}—\underset{|}{CH_2}} + NaOC_2H_5 = {}^{CH_3}_{CH_3}{>}C{=}\overset{CO_2C_2H_5}{\overset{|}{C}}—\underset{\underset{CO_2Na}{|}}{CH_2} + C_2H_5OH$$

Alkylitaconic acids when heated alone are converted into the anhydrides of alkylcitraconic acids. Alkylcitraconic acids become changed into alkylitaconic acids when heated with water at 130–150°. This depends on the decomposition of the alkylcitraconic acids into anhydride and water below its boiling point, and the gradual transformation of this anhydride at a somewhat higher temperature into the itaconic anhydride, which takes up water to form the stable acid.

The alkylcitraconic acids are easily converted into the corresponding alkylmesaconic acids by the action of sunlight on an ether-chloroform solution of the acids to which a little bromine has been added.

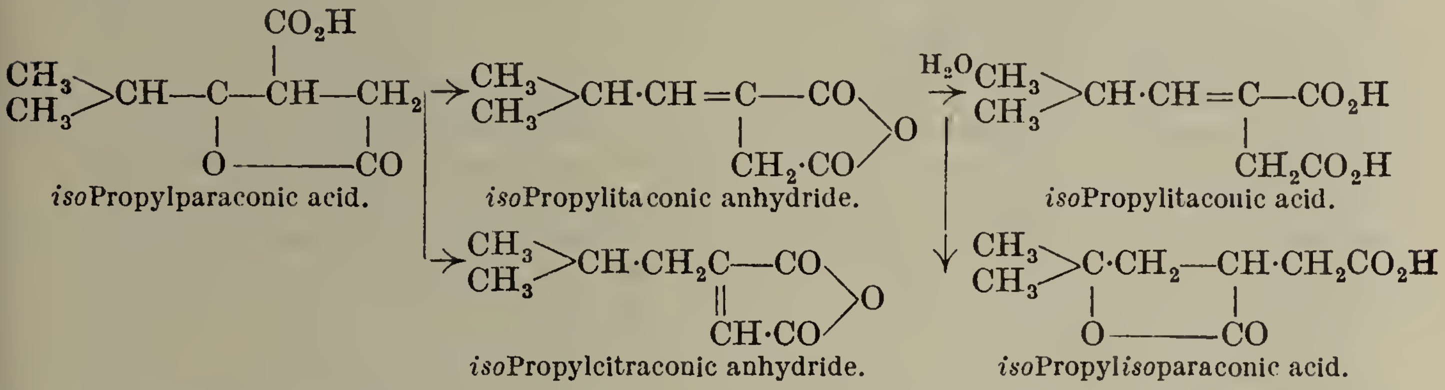
When the alkylitaconic acids are boiled with sodium hydroxide solution, the position of the double bond becomes changed, and there are produced alkylmesaconic acids and a new series of isomeric acids named by Fittig, *alkylaticonic acids* (see p. 575). The reaction is, however, not a general one, since γ-methylitaconic acid is stable towards boiling sodium hydroxide solution, whilst γ-dimethylitaconic acid readily yields the aticonic acid (Ann. **330**, 292). The alkylaticonic acids when boiled with sodium hydroxide solution pass mainly into the alkylitaconic acids, so that ultimately a point of equilibrium is reached which is not changed by further boiling.

A mixture of alkylitaconic and alkylaticonic acids (or alkylidenepyrotartaric acids) also result from the condensation of ketones, such as acetone and alkyl methyl ketone, with succinic acid ester by means of sodium methoxide (*Stobbe*, Ber. **30**, 94: Ann. **321**, 83).

Aromatic itaconic and aticonic acids can be prepared by the two nucleus-synthetic methods (Vol. II).

The alkylitaconic and alkylmesaconic acids are not volatile in steam like itaconic and mesaconic acids themselves, whilst of the alkylcitraconic acids, some are only obtained as anhydrides, and others are dissociated into the anhydride and water below 100°, like citraconic acid; these anhydrides are volatile in steam. The calcium and barium salts of the alkylmesaconic acids are readily soluble in water, whilst the corresponding alkylitaconic acid salts dissolve with difficulty.

The itaconic acids are converted into the paraconic acids, from which they were prepared, by heating with hydrochloric or hydrobromic acids and by suitable treatment with sulphuric acid. *iso*Propylitaconic acid alone behaves exceptionally, by yielding *iso*propyl*iso*paraconic acid, isomeric with the original *iso*propylparaconic acid :


*iso*Propylparaconic acid. *iso*Propylitaconic anhydride. *iso*Propylitaconic acid. *iso*Propylcitraconic anhydride. *iso*Propyl*iso*paraconic acid.

Reduction with sodium amalgam converts the alkylitaconic, alkylcitraconic, and alkylmesaconic acids into the corresponding succinic acids, the first acid reacting least readily than the third, and the second most easily of all three.

Homologous Itaconic Acids.

γ-Methylitaconic acid, $CH_3{\cdot}CH : C(COOH){\cdot}CH_2{\cdot}COOH$, m.p. 165°. *γ-Ethylitaconic acid,* m.p. 162°. *γ-*n*-Propylitaconic acid,* m.p. 159°. *γ-*iso*Propylitaconic acid,* m.p. 189°. *γ-*iso*Butylitaconic acid,* m.p. 160°. *γ-*n*-Hexylitaconic acid,* m.p. 129°. *Teraconic acid, γ-dimethylitaconic acid,* $(CH_3)_2C : C(COOH){\cdot}CH_2(COOH)$, m.p. 162°, is prepared from terebic acid (p. 612, and Vol. II) ; and by the condensation of succinic ester and acetone by means of sodium ethoxide (Ber. **36**, 197 : J. pr. Chem. [2] **67**, 197). Hydrobromic or sulphuric acid reconverts it into terebic acid ; water at 190° decomposes it into CO_2 and *iso*caprolactone (C. 1889, I. 780) ; *anhydride,* b.p. 275°. *γ-Methylethylitaconic* acid, m.p. 181° (decomp.).

α-Methylitaconic acid, $CH_2 : C(COOH){\cdot}CH(CH_3){\cdot}COOH$, m.p. 150°, is obtained from pyrocinchonic acid (below) ; *anhydride,* m.p. 63°, is produced by heating anhydromethylaconitic acid (C. 1906, II. 21).

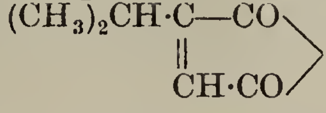
αα-Dimethylitaconic acid, $CH_2 : C(COOH){\cdot}C(CH_3)_2{\cdot}COOH$, m.p. 141°, is prepared from α-bromotrimethylsuccinic acid and diethylaniline ; *anhydride,* b.p. 210–215° ; *diethyl ester,* b.p. 127°/20 mm. (C. 1902, I. 180 : 1904, I. 434).

αγ-Dimethylitaconic acid, $CH_3CH : C(COOH){\cdot}CH(CH_3)COOH$, m.p. 202° (*anhydride,* b.p. 131°/26 mm.), and *α-ethylitaconic acid,* $CH_2 : C(COOH){\cdot}CH(C_2H_5)COOH$ (*anhydride,* m.p. 52°), result from boiling methylethylmaleic acid (p. 574) with sodium hydroxide solution ; the former also, from αγ-dimethylparaconic acid by boiling it with $NaOC_2H_5$ solution (Ber. **39**, 1535). The alkylitaconic acids mostly have no sharp melting points, owing to their tendency to form anhydrides.

Homologous Citraconic Acids, *Alkylmaleic Acids.*

γ-Methylcitraconic acid, ethylmaleic acid, $C_2H_5{\cdot}C(COOH) : CH{\cdot}COOH$, m.p. 100°, can also be obtained by heating β-ethylmalic acid (Ber. **37**, 2382 : **38**, 2737) ; *anhydride,* b.p. 229°, is obtained from ethylfumaric acid (p. 574) by heating it with acetyl chloride. When vaporized with ammonia it forms the *imide,* m.p. 141°. *γ-Ethylcitraconic acid,* n*-propylmaleic acid,* m.p. 94° ; *anhydride,* b.p. 224°. *γ-Propylcitraconic acid,* m.p. 80°. *γ-*iso*Propylcitraconic acid,* m.p. 78°. *γ-*iso*Butylcitraconic acid,* m.p. 75°. *γ-Hexylcitraconic acid,* m.p. 86°.

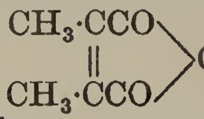
γ-Dimethylcitraconic anhydride,

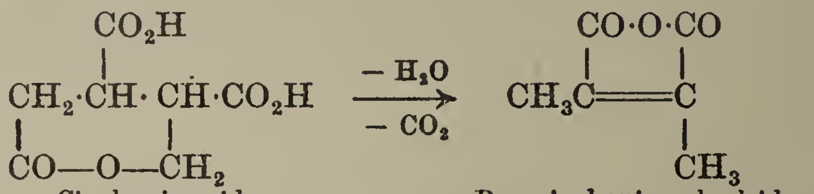


$$\begin{matrix} (CH_3)_2CH{\cdot}C{-}CO \\ \| \qquad\quad \\ CH{\cdot}CO \end{matrix}\!\!>O$$

m.p. 5°, b.p. 138°/61 mm. (C. 1899, I. 668, 780).

The γ-alkylcitraconic acids or monoalkylmaleic acids do not melt sharply on account of the formation of anhydrides. The α-alkylcitraconic or dialkylmaleic acids only exist as anhydrides, which are formed when the acid is liberated from its salts by stronger acids.

Pyrocinchonic anhydride, dimethylmaleic anhydride, α-methylcitraconic anhydride,  $\begin{matrix} CH_3\cdot CCO \\ \| \\ CH_3\cdot CCO \end{matrix}\Big>O$, m.p. 96°, b.p. 223°, is formed when cinchonic acid (*q.v.*) is heated:



Cinchonic acid. Pyrocinchonic anhydride.

It also results, together with terebic acid, when turpentine oil is oxidized with nitric acid; from α-dichloro- and α-dibromo-propionic acid and silver (Ber. **18**, 826, 835); by condensation of pyroracemic acid and sodium succinate by means of acetic anhydride (Ann. **304**, 158); by distillation of αβ-dimethylmalic acid (p. 611) under reduced pressure (a method of preparation); by distillation of anhydromethylaconitic acid (C. 1906, II. 21).

Dimethylmaleic dimethyl ester, b.p. 219°, and *diethyl ester*, b.p. 237°, are prepared from silver pyrocinchonate and iodo-alkyls (Ber. **33**, 1410). The solution of pyrocinchonic anhydride reacts strongly acid and decomposes alkali salts forming pyrocinchonates, the constitution of which has already been discussed. Ferric chloride produces a dark-red coloration in pyrocinchonic anhydride solutions. Reduction produces two dimethylsuccinic acids (p. 549). It unites with chlorine to form dichlorodimethylsuccinic anhydride (Ber. **26**, R. 190). When boiled with 20 per cent. sodium hydroxide solution, pyrocinchonic acid is converted into dimethylfumaric acid and β-methylitaconic acid (Ann. **304**, 156). Pyrocinchonic ester, when heated with alcoholic ammonia, yields aminodimethylsuccinimide (p. 611) and *pyrocinchonimide*, m.p. 119° (Ber. **33**, 1408), which on hydrolysis yields, in part, β-methylitaconic acid.

Methylethylmaleic anhydride, b.p. 236°, is formed by condensation of pyrotartaric acid and pyroracemic acid, by means of acetic anhydride (Ann. **267**, 214); by distillation of αγ-dimethylparaconic acid whereby α-methyl-βγ-pentinic acid is also formed (Ber. **39**, 1535); by the slow distillation of methylethylmalic acid; *imide*, m.p. 67°; *dimethyl ester*, b.p. 235°. The imide and anhydride can also be obtained from the destruction of hæmatin or hæmatinic acid (see hæmoglobin) (Ann. **345**, 1).

Methylpropylmaleic anhydride, b.p. 242° (*imide*, m.p. 57°) and *methyl*iso*propylmaleic anhydride*, b.p. 241° (*imide*, m.p. 45°) are obtained from methylpropyl and methyl*iso*propylmalic acid (Ann. **346**, 1).

Xeronic anhydride, diethylmaleic anhydride, b.p. 242°, is prepared by heating citraconic anhydride (Ann. **346**, 1).

Homologous Mesaconic Acids, *Alkylfumaric Acids*.—For the formation of alkylmesaconic acids from the corresponding alkylitaconic and alkylcitraconic acids, see p. 572.

The products of reaction of alcoholic potassium hydroxide and the γ-dibromo-derivatives of monoalkylacetoacetic esters belong to the alkylfumaric acid series (C. 1899, I. 780); hydroxytetrinic acid being mesaconic acid, and hydroxypentinic acid being ethylfumaric acid, etc. (p. 476).

The reaction is most simply explained by the assumption that keto- or hydroxyaldehydic acids are first formed, which are then converted into unsaturated carboxylic acids (Ber. **32**, 1005):

$$\begin{tikzcd} X_2CH\cdot COCHR'\cdot CO_2R \arrow[r] & OCH\cdot CO\cdot CHR'\cdot CO_2R \arrow[dl] \\ O\cdot CH\cdot C(OH){=}CR'\cdot CO_2R \arrow[r] & CO_2H\cdot CH : CR'\cdot CO_2R. \end{tikzcd}$$

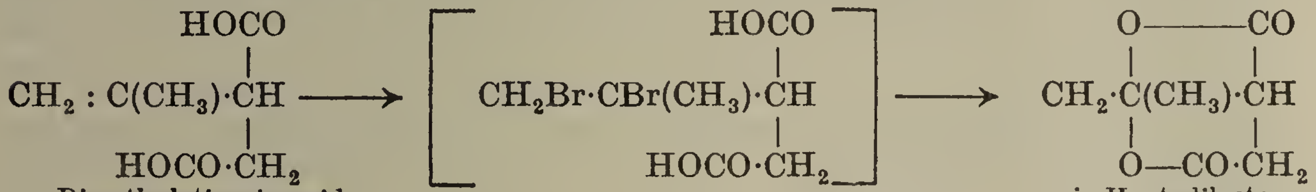
Monoalkylfumaric acids are also obtained from monoalkylethanetricarboxylic acids by the introduction of halogen and subsequent splitting off of halogen acid and CO_2 (Ber. **24**, 2008).

Ethylfumaric acid, γ-methylmesaconic acid, m.p. 194°. n.-*Propylfumaric acid, γ-ethylmesaconic acid*, m.p. 174°. iso*Propylfumaric acid, γ-dimethylmesaconic acid*, m.p. 184°. n.-*Butylfumaric acid, γ-propylmesaconic acid*, m.p. 170°. γ-iso-*Propylmesaconic acid*, m.p. 185°. γ-iso*Butylmesaconic acid*, m.p. 205°. *γ-Hexylmesaconic acid*, m.p. 153°.

Dimethylfumaric acid, α-methylmesaconic acid, m.p. 239° ; *diethyl ester,* b.p. 235°, is formed when diazopropionic ester is heated (p. 465) (Ber. **37**, 1272).

Aticonic Acids.—For the formation of these acids from the alkylitaconic acids by synthetic methods, see p. 572. *Dimethylaticonic acid,* γ-methyl-Δ^{γ}-butene-αβ-dicarboxylic acid, $\mathrm{CH_2 : C(CH_3){\cdot}CH(COOH){\cdot}CH_2COOH}$, m.p. 146°, results when teraconic acid is boiled with sodium hydroxide solution. iso*Butylaticonic acid,* ε-methyl-Δ^{γ}-hexene-αβ-dicarboxylic acid, $\mathrm{(CH_3)_2CH{\cdot}CH : CH{\cdot}CH(COOH){\cdot}CH_2(COOH)}$, m.p. 93°. *Hexylaticonic acid,* $\mathrm{CH_3({\cdot}CH_2)_4{\cdot}CH : CH{\cdot}CH(COOH){\cdot}CH_2(COOH)}$, m.p. 78° (Ann. **304**, 117 : **305**, 1). *Methylethylaticonic acid, γ-ethylidene-γ-methylpyrotartaric acid,* $\mathrm{CH_3{\cdot}CH : C(CH_3){\cdot}CH(COOH){\cdot}CH_2{\cdot}COOH}$, m.p. 142°, is the chief product of reaction between methyl ethyl ketone and sodium ethoxide on succinic ester. Oxidation converts it into acetic acid and lævulinic acid (Ann. **321**, 106).

In indifferent solvents, the alkylaticonic acids readily take up bromine. The dibromides, on losing HBr, change into the bromolactonic acids, which are converted by hydrogen into *iso*paraconic acids, and by boiling water, or when standing in alcoholic solution, into the neutral dilactones :



$$\begin{array}{c}\mathrm{HOCO}\\ |\\ \mathrm{CH_2 : C(CH_3){\cdot}CH}\\ |\\ \mathrm{HOCO{\cdot}CH_2}\end{array} \longrightarrow \left[\begin{array}{c}\mathrm{HOCO}\\ |\\ \mathrm{CH_2Br{\cdot}CBr(CH_3){\cdot}CH}\\ |\\ \mathrm{HOCO{\cdot}CH_2}\end{array}\right] \longrightarrow \begin{array}{c}\mathrm{O\text{———}CO}\\ |\qquad |\\ \mathrm{CH_2{\cdot}C(CH_3){\cdot}CH}\\ |\qquad |\\ \mathrm{O{—}CO{\cdot}CH_2}\end{array}$$

Dimethylaticonic acid. *iso*Heptodilactone.

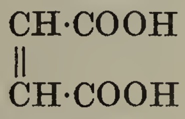
The formation of dilactones requires that each of the two doubly bound carbon atoms shall stand in the γ-position to one of the two carbonyl groups (Ann. **304**, 135). This shows the alkylaticonic acids to be γδ-unsaturated acids. It follows, therefore, that an aticonic acid isomeric with itaconic acid itself is theoretically not possible, since this acid lacks the δ carbon atom. The aticonic acids can be looked on as being vinylsuccinic acids, or can be derived from pyrotartaric acid, considerations which are indicated in the names given to the dimethylaticonic acids.

The dilactones, obtained from the aticonic acids through the bromolactonic acids, are converted by prolonged boiling in water into isomeric unsaturated lactonic acids, known as *isaconic acids.* Sodium amalgam converts them into *iso*paraconic acids, in the same way that the better-known aconic acids give paraconic acids.

Glutaconic acid, $\mathrm{CO_2H{\cdot}CH : CH{\cdot}CH_2{\cdot}CO_2H}$, m.p. 132°, is prepared from dicarboxyglutaconic ester by hydrolysis with hydrochloric acid (Ann. **222**, 249) ; from coumalic ester and barium hydroxide (Ann. **264**, 301) ; from β-hydroxyglutaric acid (p. 614), and sodium hydroxide solution (Ber. **33**, 1452). It is isomeric with itaconic, citraconic, mesaconic and ethylidene malonic acids.

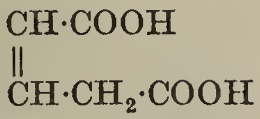
Constitution of Glutaconic Acid and the Alkylglutaconic Acids.—Constitutionally, glutaconic acid (II) occupies an intermediate position between fumaric (I) and muconic acid (III) :

(I)



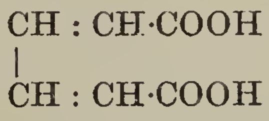
$$\begin{array}{l}\mathrm{CH{\cdot}COOH}\\ \|\\ \mathrm{CH{\cdot}COOH}\end{array}$$

(II)



$$\begin{array}{l}\mathrm{CH{\cdot}COOH}\\ \|\\ \mathrm{CH{\cdot}CH_2{\cdot}COOH}\end{array}$$

(III)



$$\begin{array}{l}\mathrm{CH : CH{\cdot}COOH}\\ |\\ \mathrm{CH : CH{\cdot}COOH}\end{array}$$

In consequence of the double linkage two stereoisomeric glutaconic acids would be expected. However, the fortuitous arrangement of the carboxyl groups, permitting of the formation of the favoured conjugated system, permits of an oscillation of the double bond as follows :

$$\mathrm{COOH{\cdot}CH : CH{\cdot}CH_2{\cdot}COOH} \rightleftarrows \mathrm{COOH{\cdot}CH_2{\cdot}CH : CH{\cdot}COOH.}$$

This lability explains why only one form of glutaconic acid, presumably that favoured by energy considerations, is known (*Feist,* Ann. **428**, 29).

Stabilization of the glutaconic acid molecule occurs in the alkylglutaconic acids, in which the influence of one carboxyl group is strengthened by the presence of the alkyl group. In the α-alkylglutaconic acids (*q.v.*) the double bond is fixed in the αβ-position, and geometrical isomers appear : they are also known in the majority of β-alkylglutaconic acids. It should be noted that reactions which should yield respectively an α- and γ-alkylglutaconic acid actually yield the same substance : γ-alkylglutaconic acids do not exist (see p. 576).

The *zinc salt* is deposited from its boiling solution; *ethyl ester*, b.p. 237°, is most readily obtained by distillation of β-acetoxyglutaric ester (p. 614). Under certain conditions it polymerizes to a dimolecular substance which, on hydrolysis, yields *diglutaconic acid* $[C_3H_4(CO_2H)_2]_2$, m.p. 207°. This acid is also formed by hydrolysing the dimolecular isaconitic ester (*q.v.*), whilst the dimolecular glutaconicdicarboxylic ester (*q.v.*) yields a *diglutaconic acid*, m.p. 234° (Ber. **34**, 675). When warmed with sodium ethoxide two molecules of glutaconic ester unite with the loss of alcohol, and there is formed *dicarboxycyclohexenoneacetic ester* (Ber. **37**, 2113, *cf.* C. 1903, I. 960).

Glutaconic anhydride, m.p. 82°, is formed when glutaconic and β-hydroxyglutaric acids are heated (Kekulé); and from glutaconic acid and acetyl chloride (m.p. 87°, Ber. **27**, 882); the *imide*, *αα-dioxypyridine*, $CH\lessdot\begin{smallmatrix}CH\cdot CO\\CH_2\cdot CO\end{smallmatrix}\gtrdot NH$ or $CH\lessdot\begin{smallmatrix}CH—C(OH)\\CH=C(OH)\end{smallmatrix}\gtrdot N$, m.p. 183°, is formed (1) from glutaconaminic acid; (2) from glutaconamide, and (3) from β-hydroxyglutaric amide, when these are heated with H_2SO_4 to 130–140°. Na and CH_3I react with it to produce glutaconic methylimide; with nitrous acid it gives rise to a nitroso-compound; when distilled over zinc dust pyridine is formed: PCl_5 produces pentachloropyridine, C_5Cl_5N (see Constitution of Pyridine, Vol. II).

β-Chloroglutaconic acid, m.p. 129°, is prepared from acetonedicarboxylic acid and PCl_5 (p. 623; *cf.* glutinic acid, p. 578). *Tetrachloroglutaconic acid*, m.p. 109–110° (Ber. **26**, 2697).

Homologous Glutaconic Acids.—(1) The alkylated glutaconic acids, similarly to glutaconic acid itself, are best obtained by heating the acetyl compounds of the alkylated β-hydroxyglutaric acids (*cf.* C. 1903, II. 1313).

(2) The CH_3-group of the glutaconic ester is replaceable by alkyl groups by means of sodium or sodium alcoholate and iodoalkyls. A CH_2-group linked to $\cdot CH : CH\cdot$ and $\cdot COOC_2H_5$ possesses the same reactivity as the methylene group in a 1 : 3-diketo compound:

$$CH_2\lessdot\begin{smallmatrix}CH : CHCO_2R\\CO_2R\end{smallmatrix} \quad\text{and}\quad CH_2\lessdot\begin{smallmatrix}CO_2R\\CO_2R\end{smallmatrix}$$

Glutaconic ester. Malonic ester.

The reaction with C_2H_5ONa and CH_3I not only converts glutaconic ester into αα-dimethylglutaconic ester, but also produces αγ-dimethylglutaconic ester on account of the existence of the two desmotropic forms I and II (see below): further methylation results in the production of ααγ-trimethylglutaconic ester (C. 1903, I. 1405):

I. $RO_2C\cdot CH(CH_3)—CH=CHCO_2R$ and II. $RO_2C\cdot C(CH_3)=CH—CH_2CO_2R$

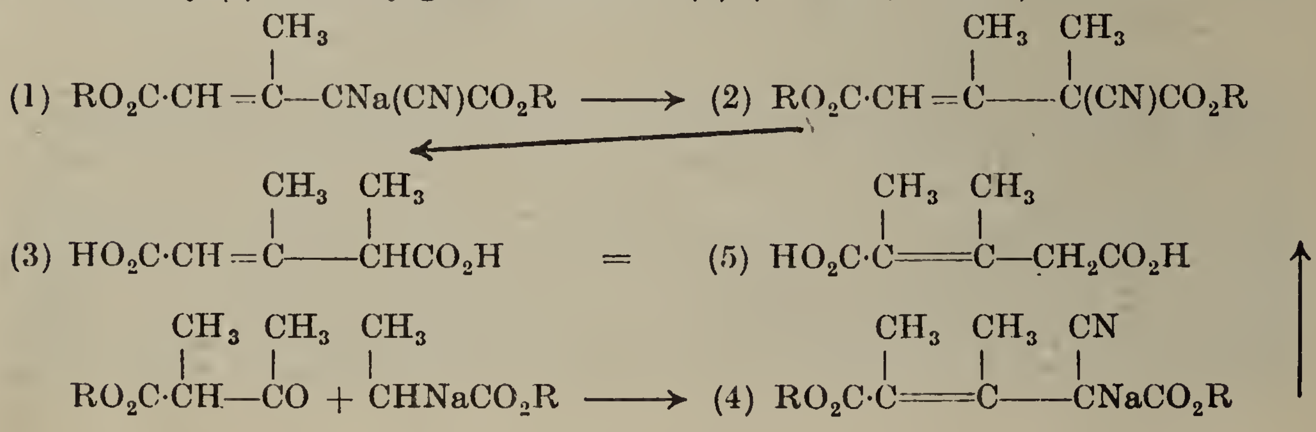
$\downarrow$ $\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad$ $\downarrow$

$RO_2C\cdot C(CH_3)_2—CH=CHCO_2R$ $\qquad$ $RO_2C\cdot C(CH_3)=CH—CH(CH_3)CO_2R$

$\downarrow$

$RO_2C\cdot C(CH_3)=CH—C(CH_3)_2CO_2R.$

(3) The identity of the two desmotropic modifications $HO_2C\cdot CR=CH—CH_2\cdot CO_2H$ and $HO_2C\cdot CHR—CH=CHCO_2H$ is also demonstrated by the identity of the αβ- and βγ-dialkylglutaconic acids, obtained by the following syntheses: sodium cyanoacetic ester and acetoacetic ester produce sodium cyano-β-methylglutaconic ester (1); CH_3I converts this into α-cyano-αβ-dimethylglutaconic ester (2), which by hydrolysis and loss of CO_2 is changed into αβ-dimethylglutaconic acid (3). This substance is identical with the decomposition product of the condensation of cyanoacetic ester and α-methyl acetoacetic ester (4), which should be similarly βγ-dimethylglutaconic acid (5) (C. 1906, I. 183):



$$\text{(1) } RO_2C\cdot CH=\overset{CH_3}{\overset{|}{C}}—CNa(CN)CO_2R \longrightarrow \text{(2) } RO_2C\cdot CH=\overset{CH_3}{\overset{|}{C}}——\overset{CH_3}{\overset{|}{C}}(CN)CO_2R$$

$$\text{(3) } HO_2C\cdot CH=\overset{CH_3}{\overset{|}{C}}——\overset{CH_3}{\overset{|}{C}}HCO_2H \;=\; \text{(5) } HO_2C\cdot\overset{CH_3}{\overset{|}{C}}==\overset{CH_3}{\overset{|}{C}}—CH_2CO_2H$$

$$RO_2C\cdot\overset{CH_3}{\overset{|}{C}}H—\overset{CH_3}{\overset{|}{C}}O + \overset{CH_3}{\overset{|}{C}}HNaCO_2R \longrightarrow \text{(4) } RO_2C\cdot\overset{CH_3}{\overset{|}{C}}==\overset{CH_3}{\overset{|}{C}}——\overset{CN}{\overset{|}{C}}NaCO_2R$$

The alkylglutaconic acids shows *cis-trans* isomerism.

A general method for the preparation of β-alkylglutaconic esters depends on the addition of ethyl sodiomalonate or sodiocyanoacetate to compounds of the type of tetrolic ester (J. pr. Chem. [2] **49**, 20).

β-Methylglutaconic acid, homomesaconic acid, $HO_2C{\cdot}CH : C(CH_3){\cdot}CH_2CO_2H$. *Cis*-form, 147°, *trans*-form, 116°, is prepared from cyano-β-methylglutaconic ester (see below); from carboxy-β-methylglutaconic ester, $(CO_2R)_2CH{\cdot}C(CH_3) : CHCO_2R$; and from *iso*dehydracetic acid (lactone of aci-acetyl-β-glutaconic monoester, $CH_3C(OH) : (CO_2R){\cdot}C(CH_3) : CHCO_2H$). It can be split into the *cis-* and *trans*-forms. The *cis*-acid can be transformed into the *trans*-acid by boiling with strong alkali. The *cis*-acid forms as *anhydride,* m.p. 86°; *imide,* m.p. 194° (Ann. **345**, 60).

αβ- or *βγ-Dimethylglutaconic acid* (see above), m.p. 148°, is formed by the method (3), above; also from β-methylglutaconic ester by the action of sodium and iodomethane (Ann. **345**, 117); *anhydride,* b.p. 162°/25 mm.; *imide,* m.p. 189°.

αα-Dimethylglutaconic acid, $HO_2C{\cdot}C(CH_3)_2CH : CHCO_2H$, *cis*-form, m.p. 134°; *trans*-form, m.p. 172°, is prepared from α-dimethylglutolactonic acid (Ber. **33**, 1920); from β-hydroxy-α-dimethylglutaric acid; from glutaconic ester, sodium and iodomethane; some *αγ-dimethylglutaconic acid,* m.p. 147°, is also formed (above) (C. 1903, II. 1315).

ααγ-Trimethylglutaconic acid, cis-form, m.p. 125°, *trans*-form, m.p. 150°, is formed from β-hydroxytrimethylglutaric acid and by methylating αγ-dimethylglutaric acid. The *cis*-acid gives rise to an *anhydride,* m.p. 88°.

ααβ-Trimethylglutaconic acid, cis-form, m.p. 133°, *trans*-form, m.p. 148° (C. 1903, II. 1315). *αβγ-Trimethylglutaconic acid,* m.p. 127°; *anhydride,* m.p. 119°; *imide,* m.p. 180° (C. 1906, I. 185).

Hydromuconic Acids.

αβ-acid : $CO_2H{\cdot}CH_2CH_2CH{=}CHCO_2H$, m.p. 169°, *stable* form.
βγ-acid : $CO_2H{\cdot}CH_2CH{=}CH{\cdot}CH_2CO_2H$, m.p. 195°, *labile* form.

The *labile* acid is formed by the reduction of dichloromuconic acid or muconic acid (below), and of diacetylenecarboxylic acid (p. 578). It dissolves with difficulty in cold water, and is oxidized to malonic acid by potassium permanganate. When boiled with sodium hydroxide solution it is transformed into the *stable* acid, which is oxidized to succinic acid by permanganate. Sodium amalgam converts the labile acid into the stable form and reduces this to adipic acid (p. 561). *Dichlorides* and *dimethylene ester* (C. 1901, II. 1119).

α-Methyleneglutaric acid, $CH_2 : C(COOH)CH_2{\cdot}CH_2CO_2{\cdot}H$, m.p. 129–130°, and *α-ethylidene-β-methylglutaric acid,* $CH_3{\cdot}CH : C(CO_2H)CH(CH_3)CH_2CO_2H$, m.p. 129°. The esters of these acids are obtained by the polymerization of acrylic and crotonic acids respectively (pp. 342, 344) by means of sodium alcoholate (Ber. **33**, 3766 : **34**, 427). α-Methyleneglutaric acid is also formed by the distillation of α-methyl-α-hydroxyvaleric acid (Ber. **36**, 1202). Suitable methods of reduction convert these acids into α-methylglutaric acid and α-ethyl-β-methylglutaric acid respectively.

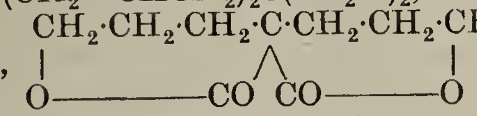
α-Ethylideneglutaric acid, $CH_3CH : C(COOH)CH_2CH_2CO_2H$, m.p. 152°, see δ-caprolactone carboxylic acid (p. 615). Sodium hydroxide solution converts it into *α-vinylglutaric acid,* $CH_2 : CH{\cdot}CH(CO_2H)CH_2CH_2CO_2H$, m.p. 97° (Ber. **31**, 2000).

iso*Amylideneglutaric acid,* $(CH_3)_2CHCH_2CH : C(CO_2H)CH_2CH_2CO_2H$, m.p. 75°, is formed together with di*iso*valerylideneglutaric acid (see below).

Allylsuccinic acid, $CH_2 : CH{\cdot}CH_2CH(CO_2H)CH_2CO_2H$, m.p. 94°, is prepared from allyl ethane tricarboxylic ester (Ber. **16**, 333). *Allylmethyl-* and *allylethylsuccinic acid,* see Ber. **25**, 488.

C. DIOLEFINE DICARBOXYLIC ACIDS

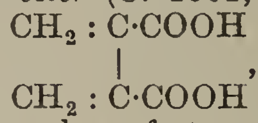
Diallylmalonic acid, $(CH_2{=}CHCH_2)_2C(CO_2H)_2$, m.p. 133°, with hydrobromic acid yields a dilactone,



$$\begin{array}{l} CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2 \\ \;|\qquad\qquad\qquad\quad \wedge \qquad\qquad\quad | \\ O \text{———} CO\;\;CO \text{———} O \end{array}$$

. It breaks down into CO_2 and diallylacetic acid when heated (p. 354).

Muconic acid, $CO_2H{\cdot}CH{=}CH{-}CH{=}CH{\cdot}CO_2H$, m.p. 292° (decomp.) (*Configuration,* see Ber. **49**, 999, and Ann. **418**, 294), is formed when alcoholic potassium hydroxide acts on the dibromide of $\beta\gamma$-hydromuconic acid ; also, synthetically, from glyoxal and two molecules of malonic acid by means of pyridine. Oxidation produces chiefly tartaric acid, with a little mucic acid (Ann. **418**, 294) ; *dimethyl ester*, m.p. 158° (Ber. **35**, 1147). *Dichloromuconic acid*, $C_6H_4Cl_2O_4$, results when PCl_5 acts on mucic acid (Ber. **24**, R. 629). It yields $\beta\gamma$-hydromuconic acid with sodium amalgam (Ber. **23**, R. 232). *Dichloromuconic acid dichloride, and dimethyl ester* (C. 1901, II. 1119).

Dimethylenesuccinic acid, 

$$\begin{array}{c}CH_2 : C{\cdot}COOH\\ |\\ CH_2 : C{\cdot}COOH\end{array}$$

, may be considered as being the parent substance of a large number of strongly coloured well-crystallizing acids of the aromatic series (Vol. II). It easily passes into a more deeply coloured anhydride, and exhibits a reversible difference of state in violet and ultra-violet light (p. 82). Therefore Stobbe named the hypothetical acid *fulgenic acid* (fulgere = to shine) and the anhydride *fulgide*. The lesser-known aliphatic fulgenic acids and fulgides are colourless (Ann. **359**, 1, etc.).

*Di*iso*propylidenesuccinic acid*, *$\alpha\alpha\delta\delta$-tetramethylfulgenic acid*, $(CH_3)_2C : C(COOH){\cdot}C(COOH) : C(CH_3)_2$, m.p. 230° (decomp.), and iso*propylidene*iso*butylidenesuccinic acid*, *$\alpha\alpha\delta$-dimethyl*iso*propylfulgenic acid*, $(CH_3)_2C : C(COOH)C(COOH) : CHCH(CH_3)_2$, m.p. 226° (decomp.), result from the reaction of teraconic ester and acetone or *iso*butylaldehyde respectively, with sodium ethoxide. The *anhydrides*, m.pp. 59° and 72°, are formed by means of acetyl chloride (Ber. **38**, 3673, 3683).

*Di*iso*valeralglutaric acid*, $CH_2[C(CO_2H) : CHCH_2CH(CH_3)_2]_2$, m.p. 220°, and is obtained from glutaric acid and *iso*valeraldehyde with acetic anhydride and sodium ethoxide or sodium (Ann. **282**, 357).

D. ACETYLENE AND POLYACETYLENE DICARBOXYLIC ACIDS

Acetylenedicarboxylic acid, $CO_2H{\cdot}C{\equiv}C{\cdot}CO_2H + 2H_2O$, m.p. 175° (decomp.), is obtained when aqueous or alcoholic potassium hydroxide acts on dibromo- and *iso*dibromo-succinic acid (Ann. **272**, 127). It effloresces on exposure. The anhydrous acid crystallizes from ether in thick plates. The acid unites with the halogen acids to form halogen fumaric acids, whilst with bromine and iodine it yields dihalogen fumaric acids (p. 570). Its esters unite with bromine and form dibromomaleic esters and dibromofumaric esters (Ber. **25**, R. 855). With water they yield oxaloacetic ester (Ber. **22**, 2929). They combine with phenylhydrazine and hydrazine, forming the same pyrazolone derivatives as oxalacetic ester (Ber. **26**, 1719) ; and with diazobenzene imide they form phenyltriazole dicarboxylic ester (Ber. **26**, R. 585). Oxaloacetic ester and acetylene dicarboxylic ester are condensed by alcoholic potassium hydroxide to aconitic ester (Ber. **24**, 127). (See also Acetoxymaleic anhydride, p. 620.) The primary *potassium salt*, C_4O_4HK, is not very soluble in water, and when heated decomposes into CO_2 and potassium propiolate (p. 351) ; *silver salt* breaks down readily into CO_2 and silver acetylide (Ann. **272**, 139) ; *diethyl ester*, b.p. 145–148°/15 mm., is obtained from dibromosuccinic ester with sodium ethoxide (Ber. **26**, R. 706). (See also Thiophentetracarboxylic esters (Vol. III).

Glutinic acid, $CO_2H{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CO_2H$, m.p. 145° with evolution of carbon dioxide, is obtained by the action of alcoholic potassium hydroxide (Ber. **20**, 147) upon chloroglutaconic acid (p. 576).

Diacetylenedicarboxylic acid, $CO_2H{\cdot}C{\equiv}C{-}C{\equiv}C{\cdot}CO_2H + H_2O$, is made by the action of potassium ferricyanide on the copper compound of propiolic acid (Ber. **18**, 678, 2269). It assumes a dark-red colour on exposure to light, and at 177° explodes. Sodium amalgam reduces it to hydromuconic acid, and at the same time produces some adipic and propionic acid. *Ethyl ester*, b.p. 184°/200 mm. Zinc and hydrochloric acid decompose it and yield propargylic ester (p. 351).

Tetraacetylenedicarboxylic acid, $CO_2H{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CO_2H$. Carbon dioxide escapes on digesting the acid sodium salt of diacetylenedicarboxylic acid with water, and there is formed the sodium salt of diacetylenemonocarboxylic acid, $CH{\equiv}C{\cdot}C{\equiv}CO_2Na$, which cannot be obtained in a free condition. When potassium ferricyanide acts on the copper compound of this acid, tetraacetylenedicarboxylic acid is formed. This crystallizes from ether in beautiful needles, rapidly darkening on exposure to light and exploding violently when heated. Consult Ber. **18**, 2277, for an experiment made to explain the explosibility of this derivative.

V. TRIHYDRIC ALCOHOLS: GLYCEROLS AND THEIR OXIDATION PRODUCTS

The trihydric alcohols, or glycerols, and their oxidation products are connected with the dihydric alcohols (glycols) and their oxidation products.

The glycerols, so-called after their most important member, are obtained from the hydrocarbons by the substitution of three hydroxyl groups for three hydrogen atoms, linked to different carbon atoms. As the number of hydroxyl groups increases, the number of theoretically possible classes of glycerols, in contrast to the glycols, also becomes greater. The number of possible classes of oxidation products also grows accordingly, and in the case of the trihydric alcohols this number is 19. Many of the theoretically possible oxidation products of the trihydric alcohols are only obtained with difficulty, and representatives of some classes are practically unknown.

1. TRIHYDRIC ALCOHOLS

Glycerol stands at the head of this class, although it is not a triprimary alcohol, but a diprimary-secondary alcohol. The simplest imaginable triprimary alcohol would have the formula $CH(CH_2OH)_3$, and could be referred to trimethylmethane, $CH(CH_3)_3$, whereas glycerol is derived from propane, and considering the structure of the carbon nucleus, it is the simplest trihydric alcohol.

Three hydrogen atoms in glycerol can be replaced by alcohol or acid radicals, producing ethers and esters:

$C_3H_5(OH)_2(OCOCH_3)$	$C_3H_5(OH)(OCOCH_3)_2$	$C_3H_5(OCOCH_3)_3$
Monoacetin.	Diacetin.	Triacetin.

The halogen esters are the halohydrins:

$C_3H_5(OH)_2Cl$	$C_3H_5(OH)Cl_2$	$C_3H_5Cl_3$
Monochlorohydrin.	Dichlorohydrin.	Trichlorohydrin.

A well-known property of glycerol is its ability to raise the conductivity of aqueous boric acid solutions. This property, which is not exhibited by glycol, is well developed in glycerol, and is even more pronounced in the higher polyhydric alcohols, *e.g.* mannitol. Investigation has shown that only spatially adjacent hydroxyl groups bring about this increase in conductivity. Boeseken has shown that this effect is probably due to the formation of cyclic boric ester-acids, and in his hands has been of value in the elucidation of the configuration of polyglycols (Z. anorg. Chem. **142,** 83): see also α- and β-glucose, p. 693.

Formation.—The trihydric alcohols are obtained (1) by heating the bromides of the unsaturated alcohols with water; or—

(2) By oxidizing the unsaturated alcohols with potassium permanganate (Ber. **28,** R. 927).

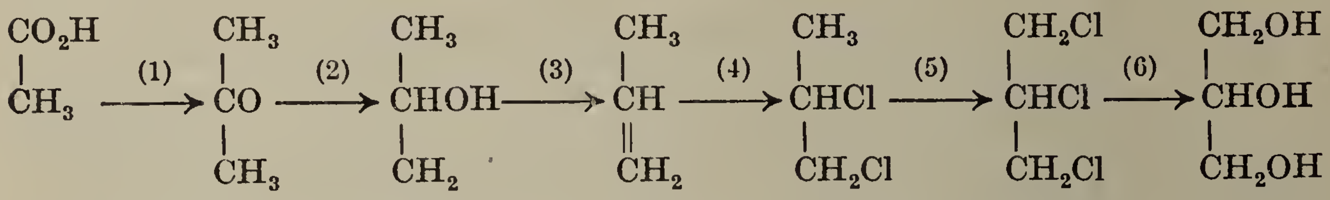
(3) Aldehydes having the constitution RCH_2CHO condense with formaldehyde in the presence of lime to form triprimary glycerols:

$$RCH_2CHO + 3CH_2O + H_2O = RC(CH_2OH)_2CH_2OH + HCOOH.$$

(4) Dialkyl ethers of glycerol are prepared by the magnesium organic synthesis from carboxylic esters or alkoxyketones and chloro- or iodo-substituted ethers.

Glycerol [propanetriol], $CH_2OH{\cdot}CHOH{\cdot}CH_2OH$, is produced (1) in small quantities in the alcoholic fermentation of sugar; hence is contained in wine (p. 141). By the addition of sodium sulphite to the fermentation, it is possible to increase markedly the formation of glycerol (*Connstein and Lüdecke*, Ber. **52,** 1385: see p. 141). (2) It is prepared by hydrolysis of oils and fats, which are glycerol esters of the fatty acids. (3) From synthetic allyl trichloride by heating it with water. (4) From allyl alcohol when it is oxidized with potassium permanganate. (5) By the reduction of dihydroxyacetone.

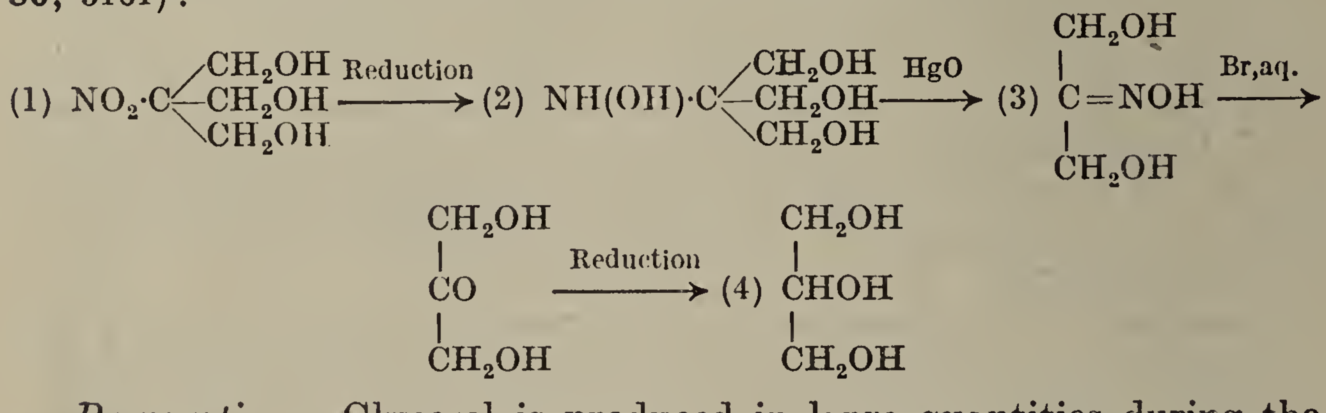
Historical.—Scheele discovered glycerol in 1779, when he saponified olive oil with litharge, in making lead plaster. *Chevreul,* who recognized ester-like derivatives of glycerol in the fats and fatty oils, introduced the name glycerol, and in 1813 pointed to similarities between it and alcohol. The composition of glycerol was established in 1836, by *Pelouze. Berthelot* and *Lucca* (1853), and later *Wurtz* (1855), explained its constitution, and proved that it was the simplest trihydric alcohol, the synthesis of which *Friedel* and *Silva* (1872) effected from acetic acid:



$$\begin{array}{ccccccccccccc} CO_2H & & CH_3 & & CH_3 & & CH_3 & & CH_3 & & CH_2Cl & & CH_2OH \\ | & & | & & | & & | & & | & & | & & | \\ CH_3 & \xrightarrow{(1)} & CO & \xrightarrow{(2)} & CHOH & \xrightarrow{(3)} & CH & \xrightarrow{(4)} & CHCl & \xrightarrow{(5)} & CHCl & \xrightarrow{(6)} & CHOH \\ & & | & & | & & \| & & | & & | & & | \\ & & CH_3 & & CH_2 & & CH_2 & & CH_2Cl & & CH_2Cl & & CH_2OH \end{array}$$

(1) Acetone is obtained from calcium acetate. (2) Acetone by reduction passes into *iso*propyl alcohol. (3) Propylene results when anhydrous zinc chloride withdraws water from *iso*propyl alcohol. (4) Chlorine and propylene yield propylene chloride. (5) Propylene chloride and iodine chloride react to form propenyl trichloride or allyl trichloride, the trichlorohydrin of glycerol. (6) Glycerol is produced when trichlorohydrin is heated with much water to 160° (Ber. **6,** 969). Metallic iron and bromine convert propylene bromide into tribromohydrin, which silver acetate changes to triacetin. Bases saponify the latter and glycerol results (Ber. **24,** 4246).

A second method of synthesizing glycerol is that of *O. Piloty* (1897), which starts from *L. Henry's* nitro-*tert.*-butyl glycerol, the condensation product of formaldehyde and nitromethane. (1) Nitro-*tert.*-butyl glycerol is reduced to hydroxylamino-*tert.*-butyl glycerol, which is then (2) oxidized by HgO to dihydroxyacetone oxime: (3) bromine water converts this substance into dihydroxyacetone: which, finally, is reduced to glycerol by sodium amalgam (Ber. **30,** 3161):



$$(1)\ NO_2{\cdot}C\begin{cases} CH_2OH \\ CH_2OH \\ CH_2OH \end{cases} \xrightarrow{\text{Reduction}} (2)\ NH(OH){\cdot}C\begin{cases} CH_2OH \\ CH_2OH \\ CH_2OH \end{cases} \xrightarrow{\text{HgO}} (3)\ \begin{array}{c} CH_2OH \\ | \\ C{=}NOH \\ | \\ CH_2OH \end{array} \xrightarrow{\text{Br,aq.}}$$

$$\begin{array}{c} CH_2OH \\ | \\ CO \\ | \\ CH_2OH \end{array} \xrightarrow{\text{Reduction}} (4)\ \begin{array}{c} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

Preparation.—Glycerol is produced in large quantities during the saponification of fats and oils in soap and candle manufacture. When the process is carried out with superheated steam, an aqueous solution of glycerol and free insoluble fatty acids are formed. Pure glycerol is produced from its solution by distillation under reduced pressure. The hydrolysis of fats can also be brought about by heating with sulphuric acid, with alkalis ($Ca(OH)_2$) or by the employment of enzymes (*Lipases*).

Properties.—Anhydrous glycerol is a thick, colourless syrup, which slowly solidifies at 0°, forming transparent crystals, m.p. 17°, b.p. 290°, b.p. 170°/12 mm., $D_{15} = 1{\cdot}265$. With superheated steam it distils entirely unaltered. It has a pure, sweet taste, hence the name glycerol, and it is very hygroscopic, mixing in every proportion with water and alcohol. It is fairly soluble (1 : 3) in acetone (Ann. **335,** 319), but insoluble in ether. It dissolves the alkalis, alkali earths and many metallic oxides, forming with them, in all probability, metallic compounds similar to the alcoholates (p. 144). Its property of increasing the conductivity of aqueous boric acid solutions is of importance and has already been referred to (p. 579).

Copper sodium glycerate, $(C_3H_5O_3CuNa)_2 + 3H_2O$, is obtained from glycerol, copper oxide and sodium hydroxide solution (Ber. **31,** 1453).

Reactions.—(1) When glycerol is distilled with dehydrating substances, like sulphuric acid and phosphorus pentoxide, boric acid, or preferably potassium hydrogen sulphate, it decomposes into water and acrolein (p. 253).

(2) When heated to 430–450°, glycerol decomposes partly into acrolein and partly into acetol:

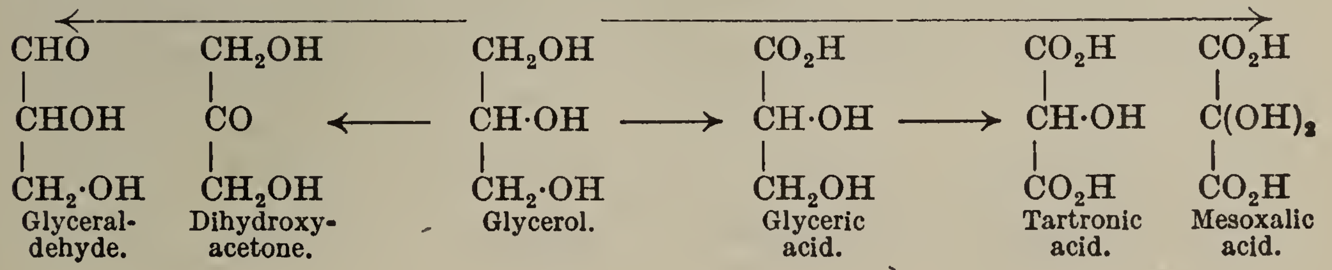
$$CH_2:CHCHO \xleftarrow{-2H_2O} CH_2(OH){\cdot}CH(OH){\cdot}CH_2(OH) \xrightarrow{-H_2O} CH_3{\cdot}CO{\cdot}CH_2OH$$

(*cf.* transformation of glycols into aldehydes and ketones, p. 361); the acetol partially decomposes into acetaldehyde and formaldehyde which, like acrolein itself, unite with glycerol to form acetal-like substances (Ann. **335,** 209).

(3) When sodium glycerol or glycerol and sodium hydroxide are heated together, hydrogen is evolved and mainly lactic acid is formed, together with lower fatty acids, methyl alcohol and propylene glycol (Ann. **335,** 279).

(4) Platinum black and air, mercuric oxide and alkali or dilute nitric acid convert glycerol into glyceric and tartronic acids; sodium and bismuth nitrate oxidize it to mesoxalic acid (Ber. **27,** R. 666). Energetic oxidation produces oxalic, glycollic and glyoxylic acids (p. 455); silver oxide gives rise to formic and glycollic acids (Ann. **335,** 316).

(5) Moderated oxidation (with nitric acid or bromine) produces *glycerose,* which consists chiefly of some glyceraldehyde and much dihydroxyacetone, $CO(CH_2{\cdot}OH)_2$. The latter unites with HCN and forms trihydroxybutyronitrile.



$$\begin{array}{cccccccccc}
\multicolumn{2}{c}{\longleftarrow} & & & & & & & & \longrightarrow \\
CHO & CH_2OH & & CH_2OH & & CO_2H & & CO_2H & & CO_2H \\
| & | & & | & & | & & | & & | \\
CHOH & CO & \longleftarrow & CH{\cdot}OH & \longrightarrow & CH{\cdot}OH & \longrightarrow & CH{\cdot}OH & & C(OH)_2 \\
| & | & & | & & | & & | & & | \\
CH_2{\cdot}OH & CH_2OH & & CH_2{\cdot}OH & & CH_2OH & & CO_2H & & CO_2H \\
\text{Glyceraldehyde.} & \text{Dihydroxyacetone.} & & \text{Glycerol.} & & \text{Glyceric acid.} & & \text{Tartronic acid.} & & \text{Mesoxalic acid.}
\end{array}$$

(6) Phosphorus iodide or hydriodic acid converts it into allyl iodide, *iso*propyl iodide, and propylene (p. 161).

(7) In the presence of yeast at 20–30° it ferments, forming propionic acid. By fermentation, induced by the *Butyl bacillus* (Ber. **30**, 451 ; **41**, 1412), normal butyl alcohol (p. 146), trimethylene glycol and formic and lactic acids result (p. 417).

(8) When glycerol is distilled with ammonium chloride, ammonium phosphates and other ammonium salts, β-picoline (Vol. III), as well as 2 : 5-dimethyl pyrazine (Vol. III), results.

(9) Reaction of glycerol with oxalic acid, see p. 282.

Uses.—Glycerol is applied as such in medicine. It is also used in gas meters. Duplicating plates and hectographs consist of mixtures of gelatin and glycerol.

The bulk of glycerol is consumed in the manufacture of nitroglycerine (p. 583).

Homologous Trihydric Alcohols

Glycerol homologues of the general formula $R\cdot CH(OH)\cdot CH(OH)\cdot CH_2OH$ can be prepared from acrolein, $CH_2 : CH\cdot CHO$, by the action of Grignard reagents, the unsaturated alcohols so formed, $CH_2 : CH\cdot CH(OH)\cdot R$, being converted into the trihydric alcohols through their dibromides (Compt. rend. **175**, 967).

Homologues of the formula $R\cdot C(CH_2OH)_3$ are obtained by the condensation of aldehydes, $R\cdot CH_2\cdot CHO$ and formaldehyde in the presence of lime :

$$R\cdot CH_2\cdot CHO + 3H\cdot CHO + H_2O \longrightarrow R\cdot C(CH_2OH)_2\cdot CH_2OH + H\cdot COOH$$

αβγ-Butanetriol, $CH_3\cdot CH(OH)\cdot CH(OH)\cdot CH_2OH$, b.p. 172–175°/27 mm., is prepared from crotonyl alcohol dibromide (p. 151).

αβγ-Pentanetriol, $C_2H_5\cdot CH(OH)\cdot CH(OH)\cdot CH_2\cdot OH$, b.p. 192°/63 mm. ; *βγδ-pentanetriol*, $CH_3\cdot CH(OH)\cdot CH(OH)\cdot CH(OH)\cdot CH_3$, b.p. 180°/27 mm. ; *β-ethylglycerol*, $CH_3\cdot CH_2C(OH)(CH_2OH)_2$, b.p. 186–189°/68 mm. These and other glycerols result upon oxidizing unsaturated alcohols with potassium permanganate (Ber. **27**, R. 165 : **28**, R. 927).

ααγγ-Tetramethylglycerol, (*βδ-dimethylpentane-βγδ-triol*) m.p. 99° (Compt. rend. **176**, 1400). Further homologues, see Compt. rend. **180**, 1408.

Pentaglycerol, $CH_3C(CH_2OH)_3$, m.p. 199°, is obtained by the action of lime on propyl aldehyde and formaldehyde (Ann. **276**, 76). *Dimethylpentaglycerol*, $(CH_3)_2CHC(CH_2OH)_3$, m.p. 83°, is prepared from *iso*valeraldehyde and formaldehyde by the action of lime (Ber. **36**, 1341). These substances are triprimary glycerols.

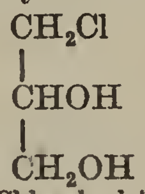
αδε-Hexanetriol, $CH_3\cdot CH(OH)\cdot CH(OH)\cdot CH_2\cdot CH_2\cdot CH_2OH$, b.p. 181°/10 mm., and some other isomers and higher homologues have been obtained from the addition products of bromine and hypochlorous acid with the corresponding unsaturated alcohols.

For unsaturated trihydric alcohols of the type $CH_2OH\cdot CHOH\cdot C \vdots C\cdot CH_2OH$, from chloroacetaldehyde and the magnesium compound of propargyl alcohol, see Compt. rend. **176**, 1068.

A. Glycerol Esters of Inorganic Acids

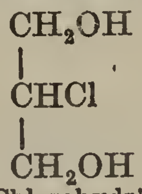
(*a*) *Halogen Esters*

These are called halohydrins (p. 369). There are two possible isomeric mono- and di-halohydrins. They are distinguished as α-halohydrins and β-halohydrins :



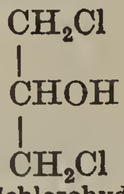
$$\begin{array}{c} CH_2Cl \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

α-Chlorohydrin.



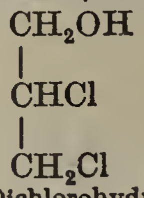
$$\begin{array}{c} CH_2OH \\ | \\ CHCl \\ | \\ CH_2OH \end{array}$$

β-Chlorohydrin.



$$\begin{array}{c} CH_2Cl \\ | \\ CHOH \\ | \\ CH_2Cl \end{array}$$

α-Dichlorohydrin.



$$\begin{array}{c} CH_2OH \\ | \\ CHCl \\ | \\ CH_2Cl \end{array}$$

β-Dichlorohydrin.

The monohalohydrins may also be regarded as halogen substitution products of propylene and trimethylene glycol, whilst the dihalohydrins are the dihalogen substitution products of propyl and *iso*propyl alcohol (p. 145).

α-Monohalohydrins are formed when the halogen acids act on glycerol, and by the interaction of water and epihalohydrins. *α-Chlorohydrin,* $CH_2OH{\cdot}CHOH{\cdot}CH_2Cl$, b.p. 139°/18 mm. *α-Bromohydrin,* b.p. 180°/10 mm. *α-Iodohydrin,* b.p. 62°/24 mm. (Ann. **335**, 237).

β-Chlorohydrin, $CH_2OH{\cdot}CHCl{\cdot}CH_2OH$, b.p. 146°/18 mm., is obtained from allyl alcohol and ClOH (C. 1897, I. 741).

α-Dihalohydrins are produced when the halogen acids (Ann. **208**, 349) act on glycerol, and on the epihalohydrins (p. 587) (Ber. **10**, 557). Potassium iodide changes the chlorine derivative into the iodine compound.

α-Dichlorohydrin, $CH_2Cl{\cdot}CHOH{\cdot}CH_2Cl$, b.p. 174°, $D_{19} = 1{\cdot}367$, is a liquid, with ethereal odour. It is not very soluble in water, but dissolves readily in alcohol and ether. When heated with hydriodic acid it becomes converted into *iso*propyl iodide; sodium amalgam produces *iso*propyl alcohol. When sodium acts on an ethereal solution of α-dichlorohydrin, we do not get trimethylene alcohol, but allyl alcohol as a result of molecular transposition (Ber. **21**, 1289). Chromic acid oxidizes it to β-dichloroacetone (p. 265) and chloroacetic acid. Potassium hydroxide converts it into epichlorohydrin (p. 587).

α-Dibromohydrin, $CH_2Br{\cdot}CHOH{\cdot}CH_2Br$, b.p. 219°; $D_{18} = 2{\cdot}11$.

α-Di-iodohydrin, $D = 2{\cdot}4$, solidifies at − 15°, is a thick oil. It readily loses HI and yields a polymeric *β-iodopropionaldehyde* (C. 1900, II. 169).

β-Ethylglycerol-α-dichlorohydrin, $C_2H_5C(OH)(CH_2Cl)_2$, b.p. 77°/15 mm., is formed from *sym.*-dichloroacetone and ethyl magnesium bromide (C. 1906, I. 1471).

The **β-Dihalohydrins** result from the addition of halogens to allyl alcohol.

β-Dichlorohydrin, b.p. 183°, $D_0 = 1{\cdot}379$, is converted by sodium into allyl alcohol. Hydriodic acid changes it to *iso*propyl iodide; fuming nitric acid oxidizes it to αβ-dichloropropionic acid.

Both dichlorohydrins are changed to epichlorohydrin by alkalis.

β-Dibromohydrin, b.p. 212–214°.

Trihalohydrins are formed when halogens are added to the allyl halides; also in the action of phosphorus halides on the dihalohydrins, and when iodine chloride acts on propylene chloride, and bromine and iron on propylene bromide and trimethylene bromide (Ber. **24**, 4246).

Trichlorohydrin, glyceryl chloride, αβγ-trichloropropane, $CH_2Cl{\cdot}CHCl{\cdot}CH_2Cl$, b.p. 158°.

Tribromohydrin, m.p. 16°, b.p. 220°, is converted by silver acetate into glycerol triacetyl ester. When this is saponified it yields glycerol (p. 580).

(*b*) *Glycerol Esters of the Mineral Acids containing Oxygen*

The neutral nitric acid ester (so-called)—*nitroglycerin* (discovered by *Sobrero* in 1847)—is the most important member of this class.

Glyceryl nitrate, "nitroglycerin," $CH_2(ONO_2){\cdot}CH(ONO_2){\cdot}CH_2(ONO_2)$, m.p. 16°, $D = 1{\cdot}6$, is produced by the action of a mixture of sulphuric and nitric acids on glycerol. The latter is added, drop by drop, to a well-cooled mixture of two parts of fuming nitric acid and three parts of concentrated sulphuric acid. On standing the nitroglycerol rises, and, after separation, is poured into water. The heavy oil (nitroglycerin) is washed with water and dried by means of calcium chloride.

Glyceryl *trinitrate* is a colourless oil, which is easily volatilized at 160°/15 mm. (Ber. 29, R. 41). It has an acrid taste, and is poisonous when taken internally. It is sparingly soluble in water, dissolves with difficulty in cold alcohol, but is easily soluble in wood spirit and ether. Heated quickly, or upon percussion, it explodes very violently; mixed with *kieselguhr* it forms *dynamite,* and with nitrocellulose, *smokeless powder.*

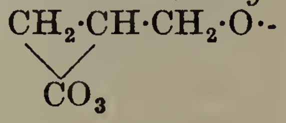
Alkalis convert nitroglycerin into glycerol and nitric acid; ammonium sulphide also regenerates glycerol. Both reactions prove that nitroglycerin is not a nitro-compound, but a nitric acid ester.

Partial nitration of glycerol or partial hydrolysis of nitroglycerin by dilute sulphuric acid produces the two possible *dinitrates,* $C_3H_5(OH)(ONO_2)_2$, oils, which are not explosive; and also the two *mononitrates,* $C_3H_5(OH)_2(ONO)_2$, m.pp. 59° and 54°; these substances are easily soluble in water (Ber. **41**, 1107).

Glyceryl nitrite, $C_3H_5(O{\cdot}NO)_3$, is formed by the action of N_2O_3 on glycerol. It is isomeric with trinitropropane (Ber. **16**, 1697).

Glycerol sulphuric acid, $CH_2OH{\cdot}CHOH{\cdot}CH_2{\cdot}OSO_3H$, is obtained from glycerol and sulphuric acid.

Carbonates of glycerol are obtained from glycerol and chloroformic ester in absolute pyridine. *Dicarbethoxyglycerol*, b.p. 162–163°/0·5 mm. *Tricarbethoxyglycerol*, b.p. 168°/0·2 mm.: *monocarbethoxyglycerol carbonate*,



$$\underbrace{CH_2{\cdot}CH}_{CO_3}{\cdot}CH_2{\cdot}O{\cdot}COOEt$$

COOEt, b.p. 304–305° (J.C.S. **125**, 2259).

Glycerophosphoric Acids, $C_3H_5(OH)_2{\cdot}O{\cdot}PO_3H_2$.—There should be theoretically two glycerophosphoric acids, the α- possessing an asymmetrical structure and capable of resolution, the β- being symmetrical and not resolvable. King and Pyman (J.C.S. **105**, 1238) have shown that the commercial crystalline sodium salt obtained from glycerol and monosodium phosphate is the β-derivative, while the acid obtained from glycerol and orthophosphoric acid at 100° under atmospheric pressure is the α-acid (*cf.* C. 1919, I. 84).

Glycerophosphoric acid occurs naturally combined with fatty acid and choline as lecithin, in yolk of eggs, brain and elsewhere (see p. 585). Willstätter and Lüdecke (Ber. **37**, 3753) find that the glycerophosphoric acid obtained from lecithin is optically active, so that it must, at any rate, partly consist of the α-acid.

B. Glycerol Fatty Acid Esters, Glycerides

(*a*) **Formic Acid Esters.** *Monoformin*, $C_3H_5(OH)_2OCHO$, distils under diminished pressure. It is formed on heating oxalic acid and glycerol (see p. 282). When heated alone it breaks down into allyl alcohol (p. 150), water, and carbon dioxide. *Diformin* is most certainly produced under these conditions. Monoformin also results from the action of α-monochlorohydrin on sodium formate. *Diformin*, $C_3H_5(OH){\cdot}(O{\cdot}CHO)_2$, b.p. 163–166°/20–30 mm.

(*b*) **Acetic esters**, or *acetins*, result when glycerol and acetic acid are heated together (C. 1897, II. 474). *Monoacetin*, b.p. 131°/2–3 mm. *Diacetin*, $C_3H_5(O{\cdot}COCH_3)_2(OH)$, b.p. 259° (Ber. **25**, 3466). *Triacetin*, $C_3H_5(O{\cdot}COCH_3)_3$, b.p. 258°, occurs in small quantities in the seed of *Euonymus europæus*, and has also been obtained from tribromohydrin (p. 583). *Dichloromonoacetin* and *monochlorodiacetin* (C. 1905, I. 12).

(*c*) **Tributyrin**, $C_3H_5(OC_4H_7O)_3$, b.p. 185°/10 mm. (C. 1899, II. 21; 1900, II. 215), occurs in cow's butter (p. 304).

(*d*) **Glycerides of higher fatty acids** occur, as already stated (p. 309), in the vegetable and animal fatty oils, fats, and tallows. They can be artificially obtained by heating glycerol with the fatty acids or their chlorides (C. 1899, II. 20), or from tribromohydrin and fatty acid salts (C. 1900, II. 215). The mono- and di-esters (monostearin, dipalmitin, etc.) are prepared from mono- (Ber. **36**, 4339: **59**, 690) or di-chlorohydrins and salts of the fatty acids, or by esterifying glycerol and the fatty acids by means of concentrated sulphuric acid (C. 1903, I. 133: Ber. **38**, 2284).

The above reactions are only to be used with caution for the determination of constitution of glycerol esters, as frequently the fatty acid residue does not enter at the position occupied by the halogen atom, probably through intermediate formation of glycidic compounds; also by the use of partially acylated glycerols, migration of the acyl groups may take place (*Fischer*, Ber. **53**, 1589, 1621). More definite conclusions can be drawn from the synthesis of monoglycerides by the action of acid chlorides in quinoline solution on glycerol-acetone (*q.v.*), the acetone residue being subsequently hydrolysed off (Ber. **53**, 1589). A similar method for the preparation of mono- and diglycerides is based on the use of the cyclic derivative of glycerol, 2-phenyl-5-hydroxymethyloxazolidone, $HO{\cdot}CH_2{\cdot}\underline{CH{\cdot}CH_2{\cdot}NH{\cdot}CH}{\cdot}C_6H_5$ (*Bergmann*, Z. physiol. Chem. **137**, 27).

By complete esterification of the mono- and diglycerides with a different fatty acid, mixed glycerides are formed, which according to recent work are the usual glycerides found in nature. A simple glyceride containing one fatty acid only is the exception rather than the rule.

αβ-Diglycerides contain an asymmetric carbon atom and can be resolved by the use of the strychnine salts of their sulphuric esters (Ber. **60**, 255). The resolution of an αβ-glyceride is the only absolutely definite method of identification from the isomeric ββ-compound.

Glycerides are sparingly soluble in alcohol, but readily soluble in ether. They are saponified by heating with alkalis or lead oxide (*cf.* p. 309, and C. 1899, II. 1699). When heated with a lower alcohol in presence of a little acid or alkali, the glycerides are largely broken down into glycerol and the ester of the alcohol employed (C. 1907, I. 151: 1908, I. 1157: II. 495).

α-*Monobenzoylglycerol*, m.p. 36°: α-*monostearin*, m.p. 81°: α-*monopalmitin*, m.p. 72°: α-*monolaurin*, m.p. 62° (E. Fischer, Ber. **53**, 1594 *et seq.*).

αβ-*Distearin*, m.p. 69°; αα-*distearin*, m.p. 79°.

Trimyristin, or myristin, glycerol myristic ester, $C_3H_5(O{\cdot}C_1\ H_{27}O)_3$, m.p. 55°, occurs in spermaceti, in nutmeg butter, and chiefly in oil nuts (from *Myristica surinamensis*), from which it is most readily obtained (Ber. **18**, 2011). It yields myristic acid (p. 306) when saponified.

Tripalmitin, $C_3H_5(O{\cdot}C_{16}H_{31}O)_3$, m.p. (45°) 65°, is found in most fats, especially in palm oil; it can be separated from olive oil at low temperatures.

Tristearin, $C_3H_5(O{\cdot}C_{18}H_{35}O)_3$, m.p. (55°) 71·5°, occurs mainly in solid fats (tallows). It can be obtained by heating glycerol and stearic acid to 280–300°. It crystallizes from ether in shining leaflets.

On the phenomenon of the "double melting point" of palmitin and stearin, see C. 1902, I. 1196.

Triolein, or olein, $C_3H_5(O{\cdot}C_{18}H_{33}O)_3$, solidifies at — 6°. It is found in oils, like olive oil. It is oxidized on exposure to the air. Nitrous acid converts it into the isomeric solid *elaidin*, m.p. 36° (p. 349).

Lecithins occur widely distributed in the animal organism, particularly in brain, nerve, blood-cells and egg-yolk (λεκιθος), from which stearo-palmito-lecithin is most easily obtained. Lecithins also occur in plant seeds (Ber. **29**, 2761). Lecithin forms a wax-like mass, readily soluble in alcohol or ether: it swells up in water and yields an opalescent solution from which it can be precipitated by various salts. The compound with cadmium chloride is characteristic and has been used for the separation of pure lecithin from eggs (J. Biol. Chem. **34**, 175: **72**, 587). It forms salts with acids and bases, and a sparingly soluble *platinichloride* $(C_{42}H_{84}NPO_8)_2H_2PtCl_6$. Lecithin is broken down when heated with alkali into choline, glycerophosphoric acid (p. 584), stearic and palmitic acids. It is to be regarded as an ester-like derivative of choline and glycerophosphoric acid (*Strecker*, Ann. **148**, 77), which is combined with stearic and palmitic acids to a glyceride: the phosphoric acid is attached to the α-hydroxyl group of the glycerol (*Willstätter* and *Lüdecke*, Ber. **37**, 3753):

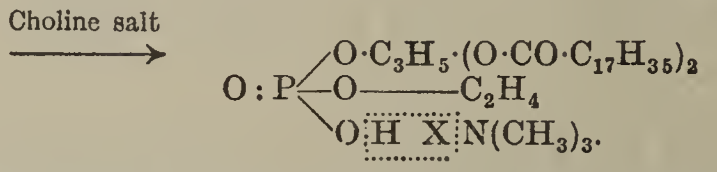
$$\begin{array}{l} CH_2{\cdot}O{\cdot}CO{\cdot}C_{17}H_{35} \\ \vert \\ CH{\cdot}O{\cdot}CO{\cdot}C_{15}H_{31} \\ \vert \\ CH_2{\cdot}O{\cdot}PO(OH){\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}N(CH_3)_3{\cdot}OH. \end{array}$$

Lecithin is optically active (dextrorotatory). When heated in alkaline solution to 90–100° it is racemized, and from the inactive lecithin, *l*-lecithin can be obtained by the employment of lipase (C. 1901, II. 193: 1906, II. 493).

In addition to the stearo-palmito-lecithin mentioned above, distearo- and dioleo- compounds are known.

Synthesis of Lecithin.—The free α-hydroxyl group of an αβ-diglyceride is esterified at its melting point by the use of phosphorus pentoxide, and by warming the product with choline salts a synthetic lecithin is obtained (*Grün* and *Limpächer*, Ber. **59**, 1530):

$$(\alpha)\ HO{\cdot}C_3H_5(O{\cdot}CO{\cdot}C_{17}H_{35})_2 \xrightarrow{P_2O_5} PO_2{\cdot}O{\cdot}PO(OH){\cdot}O{\cdot}C_3H_5(O{\cdot}CO{\cdot}C_{17}H_{35})_2$$



$$\xrightarrow{\text{Choline salt}} O:P\begin{cases} O{\cdot}C_3H_5{\cdot}(O{\cdot}CO{\cdot}C_{17}H_{35})_2 \\ O\text{———}C_2H_4 \\ O\boxed{H\ \ X}N(CH_3)_3. \end{cases}$$

The αβ-distearoylglycerol-α′-phosphoric acid choline ester is converted into its endo-salt by loss of halogen acid. Synthetic lecithin resembles in its properties (analysis, platinichloride, cadmium chloride derivative, alkaline hydrolysis) the hydrolecithin obtained by hydrogenation of natural lecithin.

So-called *β-lecithins*, where the phosphoric acid is attached to the β-hydroxyl group, have been obtained by this method, but do not occur in nature. (Endo-salt of αα′-distearoylglycerol-β-phosphoric acid choline ester, see Ber. **60**, 147.)

The **cephalins** form a series of compounds closely allied to the lecithins which occur in brain (J. Biol. Chem. **35**, 285). They contain in place of choline, β-aminoethanol. Their synthesis is carried out similarly to that of lecithin, using β-aminoethanol for the esterification of the glycerophosphoric acid in the last stage (Ber. **60**, 151).

Glycerol Ethers

1. **Alkyl ethers.**—Mixed ethers of glycerol with alcohol radicals are obtained by heating the mono- and dichlorohydrins with sodium alcoholates.

Epichlorohydrin, sodium hydroxide solution, and an alcohol form glycerol dialkyl ether (C. 1898, I. 237).

Monoethylin, $CH_2OH{\cdot}CHOH{\cdot}CH_2OC_2H_5$, b.p. 230°, is soluble in water. *Glycerol dimethyl ether*, b.p. 169°. *Diethylin*, $CH_2OH{\cdot}CH(OC_2H_5)CH_2OC_2H_5$, b.p. 191°, dissolves with difficulty in water, and has an odour resembling that of peppermint. *Triethylin*, $C_3H_5(OC_2H_5)_3$, b.p. 185°, is insoluble in water.

Glycerol allyl ether, allylin, $CH_2OH{\cdot}CHOH{\cdot}CH_2OC_3H_5$, b.p. 225–240°, is produced by heating glycerol with oxalic acid (Ber. **14**, 1946, 2270), and is present in the residue from the preparation of allyl alcohol (p. 150). *Diallylin*, $HO{\cdot}C_3H_5(OC_3H_5)_2$, b.p. 225–227°, is produced when sodium allylate acts on epichlorohydrin (Ber. **25**, R. 506).

Glycerol α-triphenylmethyl ether, m.p. 93–94°.

Higher Alkyl Ethers.—The compounds batyl, selachyl and chimyl alcohols occur in elasmobranch fish-oils, and investigation has shown that *batyl alcohol*, m.p. 69–70°, is an octadecyl ether of glycerol, $C_{18}H_{37}O{\cdot}C_3H_5(OH)_2$ (J.C.S. **1928**, 942), and *selachyl alcohol* and *chimyl alcohol* are probably the oleyl and cetyl ethers of glycerol, $C_{18}H_{35}O{\cdot}C_3H_5(OH)_2$ and $C_{16}H_{33}O{\cdot}C_3H_5(OH)_2$, respectively.

Dialkyl Ethers of Homologous Glycerols.

Fatty acid esters are condensed with chloromethyl alkyl ethers to form dialkyl ethers of homologous glycerols by means of magnesium, which can be rendered more active by means of $HgCl_2$ (C. 1907, I. 871):

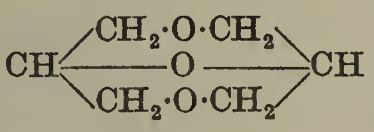
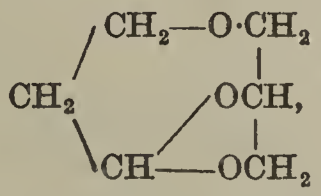
$$RCOOC_2H_5 + 2ClMgCH_2OC_2H_5 \longrightarrow RC(OH)(CH_2OC_2H_5)_2.$$

These diethylins yield acroleins, similarly to glycerol itself, when treated with oxalic acid: two molecules of alcohol are eliminated and α-alkylacroleins result (*cf.* p. 253).

Ethylglycerol diethyl ether, $C_2H_5C(OH)(CH_2OC_2H_5)_2$, b.p. 195°, is prepared from propionic ester, chloromethyl ethyl ether and magnesium. *Propylglycerol diethylin*, b.p. 210°; the iso*butyl-*, b.p. 215°; n.*-amyl-*, b.p. 119°/13 mm.; *hexyl-*, b.p. 136°/15 mm.; *octyl-*, b.p. 160°/15 mm.; *decenyl-glycerol dimethylin*, b.p. 180°/12 mm.

αη-Dimethoxyheptane-δ-ol, $HC(OH)[CH_2CH_2CH_2OCH_3]_2$, b.p. 247°, is prepared from formic ester, γ-methoxypropyl iodide and magnesium. It is a liquid possessing a very bitter taste (C. 1906, I. 332).

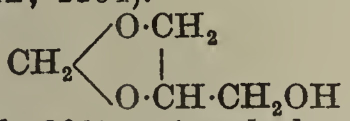
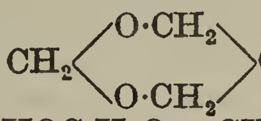
2. Cyclic Ethers :

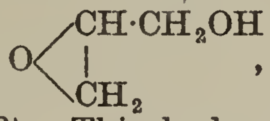
Glycerol ether,  or  b.p. 171°, is formed when glycerol is heated to 270–330°, with a little ammonium chloride (Ann. **335**, 209) ; also, together with diallylin, from epichlorohydrin and sodium allylate (see above). It is readily soluble in water, and is hydrolysed with difficulty.

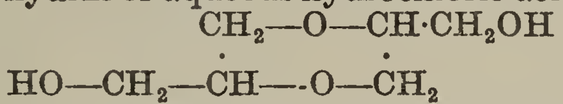
An isomeric substance, m.p. 124°, has been obtained as a by-product of the preparation of pyridine bases from glycerol and ammonium phosphate (*cf.* p. 582) (C. 1897, I. 583).

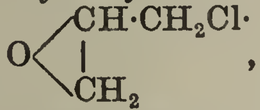
Glycerol derivatives resembling the acetals are formed when formaldehyde, acetaldehyde, acrolein, benzaldehyde, or acetone act on glycerol hot, or in presence of hydrochloric acid. The formation of the acetone compounds is of particular importance. An equilibrium exists in the following terms :

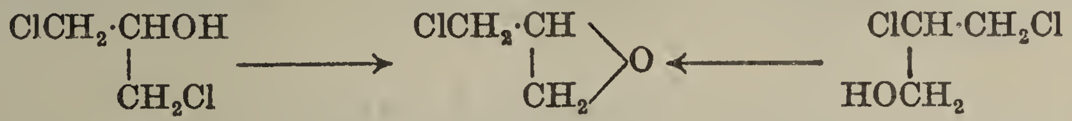
Polyhydroxylic compound + acetone ⇄ Acetone compound + water. This equilibrium is displaced more to the right according to the favourable spatial relationships of the hydroxylic groups concerned (Ber. **56**, 2409). The ease of formation of acetone compounds runs approximately parallel with the effect of the polyhydroxy compound in increasing the conductivity of boric acid solutions (Rec. Trav. Chim. **42**, 1104).

Formal glycerol,  or  b.p. 193° (Ann. **289**, 29 : **335**, 209). *Acetal glycerol*, $HOC_3H_5O_2{>}CHCH_3$, b.p. 86°/18 mm. *α-Acrolein glycerol*, $HO{\cdot}C_3H_5O_2{>}CH{\cdot}CH:CH_2$, is isomeric with glycerol ether or *β*-acrolein glycerol (*q.v.*). *Benzal glycerol*, $HOC_3H_5O_2{>}CHC_6H_5$, m.p. 66°. *Acetone glycerol*, $HOC_3H_5O_2{>}C(CH_3)_2$, b.p. 83°/11 mm. (Ber. **27**, 1536 : **28**, 1169).

Glycide Compounds : *Glycide, epihydrin alcohol*,  , b.p. 162°, $D_0 = 1{\cdot}165$, is isomeric with acetyl carbinol (p. 393). This body shows the properties both of ethylene oxide and of ethyl alcohol. It is obtained from its acetate by the action of sodium hydroxide or barium hydroxide. Glycide and its acetate reduce ammoniacal silver solutions at ordinary temperatures.

Glycerol also forms *polyglycerols*. Thus glycerol yields *diglycerol*, $(HO)_2{\cdot}C_3H_5{\cdot}OC_3H_5(OH)_2$, when it is treated with chlorohydrin or aqueous hydrochloric acid at 130°. The polymer of glycide, *diglycide*,  $\begin{matrix} & & CH_2-O-CH{\cdot}CH_2OH \\ HO-CH_2-CH-O-CH_2 \end{matrix}$ (?), results from the action of sodium acetate on epichlorohydrin in absolute alcohol, and the subsequent hydrolysis of diglycide acetate with sodium hydroxide.

Epichlorohydrin,  , b.p. 117°, $D_0 = 1{\cdot}203$, is isomeric with monochloroacetone, and constitutes the parent substance for the preparation of the glycide compounds. It is obtained from both dichlorohydrins by the action of alkali hydroxides (similarly to the formation of ethylene oxide from glycol chlorohydrin) (p. 367) :



It is a very mobile liquid, insoluble in water. Its odour resembles that of chloroform, and its taste is sweetish and burning. It forms α-dichlorohydrin with concentrated hydrochloric acid. PCl_5 converts it into trichlorohydrin. Continued heating with water to 180° changes it to α-monochlorohydrin. Concentrated nitric acid oxidizes it to β-chlorolactic acid. Metallic sodium converts it into sodium allylate, $CH_2{=}CH{\cdot}CH_2ONa$.

Like ethylene oxide, epichlorohydrin combines with HCN to the hydroxy-cyanide, $C_3H_5Cl\!<\!\begin{smallmatrix}OH\\CN\end{smallmatrix}$. *Epibromohydrin*, C_3H_5OBr, b.p. 130–140°, is prepared from the dibromohydrin. *Epi-iodohydrin*, C_3H_5OI, b.p. 62°/12 mm., is prepared from epichlorohydrin by the action of KI and alcohol, and subsequent treatment with aqueous alkali hydroxides.

Epihydrin-ether, $[O<C_3H_5]_2O$, b.p. 103°/22 mm., is produced from the above by means of silver oxide; and *nitroglycide*, $NO_2{\cdot}OC_3H_5{>}O$, b.p. 63°/15 mm., by silver nitrate. It also results when alkali acts on either of the two dinitroglycerols (p. 583) (Ann. **335**, 238: Ber. **41**, 1117).

Di-epi-iodohydrin, $ICH_2{\cdot}CH\!<\!\begin{smallmatrix}O—CH_2\\CH_2—O\end{smallmatrix}\!>\!CH{\cdot}CH_2I$, m.p. 160°, is formed when iodine acts on *mercury allyl alcohol iodide*, $(C_3H_5O{\cdot}HgI)_2$. This body, as well as *mercury propylene-glycol iodide*, $IHg{\cdot}CH_2CH(OH)CH_2OH$, is also obtained from allyl alcohol and mercury salts (*cf.* Mercury ethanol iodide, p. 370) (Ber. **34**, 1385, 2911).

Epiethylin, ethyl glycide ether, $O<C_3H_5{\cdot}OC_2H_5$, b.p. 129°, and *amyl glycide ether*, b.p. 188°, are produced from the respective ethers of chlorohydrin by distillation with potassium hydroxide (Ann. **335**, 231). *Glycide acetate*, $O<C_3H_5{\cdot}OCOCH_3$, b.p. 169°, is formed from epichlorohydrin and anhydrous potassium acetate.

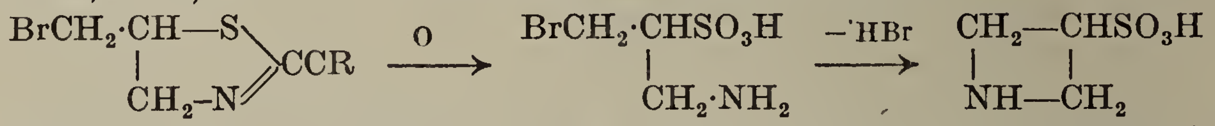
Nitrogen Derivatives of the Glycerols

*Nitro*iso*butyl glycol*, $CH_3C{\cdot}(NO_2)(CH_2OH)_2$, b.p. 140°, is formed from nitroethane and formaldehyde (Ber. **28**, R. 774).

α-Aminopropanediol, $NH_2{\cdot}CH_2CH(OH)CH_2OH$, b.p. 238°/325 mm., is formed from glycide and aqueous ammonia. Similarly, the *α-alkylaminopropanediols* can be prepared; tertiary amines react with glycerol α-chlorohydrin to form quaternary ammonium chlorides, *e.g.* $(C_2H_5)_3N(Cl)CH_2CHOH{\cdot}CH_2OH$ (Ber. **33**, 3500). *β-Aminopropanediol*, $HOCH_2{\cdot}CH(NH_2){\cdot}CH_2OH$, is formed when dihydroxyacetone oxime is reduced (Ber. **32**, 751).

β-Amino-tert.-*butanediol*, $CH_3C(NH_2)(CH_2OH)_2$ (C. 1908, I. 816).

From *αγ-diamino-β-propanol* is derived the local anæsthetic *alypin*, $C_6H_5CO{\cdot}OCH[CH_2N(CH_3)_2]_2$ (C. 1905, II. 1551); also *αγ-dianilinopropanol*, $(C_6H_5{\cdot}NHCH_2)_2CHOH$, from aniline and epichlorohydrin (Ber. **37**, 3034). *Trimethylene-imine-β-sulphonic acid* is obtained from bromomethyl taurine, a decomposition product of the thiazoline derivative obtained from allyl-mustard oil dibromide (Ber. **39**, 2891):



Triaminopropane, $CH_2NH_2{\cdot}CHNH_2{\cdot}CH_2NH_2$, b.p. 93°/9 mm., is prepared from *glyceryl triurethane*, $C_3H_5(NHCO_2C_2H_5)_3$, m.p. 92°, which is formed from the action of absolute alcohol on the triazide of tricarballylic acid (J. pr. Chem. [2] **62**, 240).

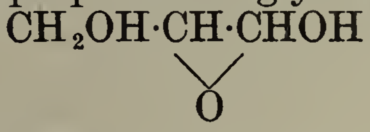
αγ-Tetramethyl-diamino-β-nitropropane, $[(CH_3)_2N{\cdot}CH_2]_2{\cdot}CHNO_2$, m.p. 58°, is prepared from 2 molecules of methanoldimethylamine, $(CH_3)_2NCH_2OH$, and nitromethane. It forms salts both with acids and alkalis (*cf.* Nitromethane, p. 181). When boiled with water it is decomposed to formaldehyde; with aqueous aniline it forms *dianilinonitropropane*, $(C_6H_5NHCH_2)_2CHNO_2$; by reduction with tin chloride it yields *ααγγ-tetramethyltriamino-propane*, $[(CH_3)_2NCH_2]_2{\cdot}CHNH_2$, b.p. 175° (Ber. **38**, 2037).

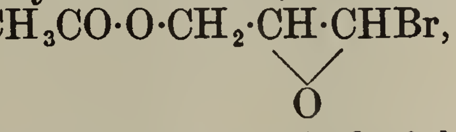
Sphingosine is a cerebroside occurring in brain tissue and has the formula $CH_3{\cdot}[CH_2]_{12}{\cdot}CH:CH{\cdot}C_3H_4(OH)_2{\cdot}NH_2$ (Z. physiol. Chem. **185**, 169: see also J. Biol. Chem. **18**, 482).

2. DIHYDROXYALDEHYDES

Glyceraldehyde [propanediolal], $CH_2OH{\cdot}CHOH{\cdot}CHO$, forms short colourless needles (from aqueous methyl alcohol), m.p. 138·5°. It is most readily obtained pure by hydrolysis of its acetal with dilute sulphuric acid (J.C.S. **1927**, 2477) and is reconverted into the acetal by treatment with alcohol and hydrochloric acid. It is almost insoluble in cold alcohol or ether. It reduces Fehling's solution in the cold, and forms a characteristic condensation product with phloroglucinol (Vol. II).

Many properties of glyceraldehyde are better explained by a cyclic formula, $CH_2OH\cdot\underset{\diagdown\,O\,\diagup}{CH\cdot CHOH}$ (Ber. **57**, 707 : **60**, 479), than by the open-chain formula, $CH_2OH\cdot CHOH\cdot CHO$, which shows analogies to the constitution of the hexoses (*q.v.*). The transformation of glyceraldehyde into dihydroxyacetone by heating in absolute pyridine is doubtless explained as occurring through the cyclic formula, and the formation of *monoacetylbromoglyceraldehyde*, $CH_3CO\cdot O\cdot CH_2\cdot\underset{\diagdown\,O\,\diagup}{CH\cdot CHBr}$, m.p. 168° (Ber. **60**, 1704), by the action of hydrobromic and glacial acetic acid on the dimeric acetate of glyceraldehyde parallels exactly the behaviour of pentaacetylglucose (*q.v.*). In the solid condition, glyceraldehyde exists in a dimolecular form (Ber. **33**, 3095).





Glyceraldehyde acetal, $CH_2OH\cdot CHOH\cdot CH(OEt)_2$, b.p. 130°/21 mm., is obtained by the careful oxidation of acraldehyde acetal (p. 254) with permanganate.

The *oxime* $CH_2OH\cdot CHOH\cdot CH : NOH$ is an oil which on warming with alkali is broken down with the formation of glycollic aldehyde by loss of water and hydrogen cyanide (*cf.* Carbohydrates).

p-*Bromophenylosazone*, m.p. 168°.

Optically Active Glyceraldehydes. Dextrorotatory—(+)—glyceraldehyde has been shown to be related to an active trihydroxybutyric acid (*l*-threonic acid) which belongs to the *l*-tartaric acid series (Ber. **50**, 455). As this belongs to the *d*-glucose series, this (+)-glyceraldehyde is correctly described as *d*-glyceraldehyde.

Preparation of optically active glyceraldehyde (Ber. **47**, 3346).

α-Chloro-β-hydroxypropionacetal, $CH_2(OH)\cdot CHCl\cdot CH(OCH_3)_2$, b.p. 98/11 mm., is formed from acrolein acetal and HClO. Oxidation converts it into α-chloro-ββ-dimethoxypropionic acid, $(CH_3O)_2CH\cdot CHClCOOH$; reaction with ammonia produces *α-hydroxy-β-aminopropionacetal*, $CH_2(NH_2)\cdot CH(OH)CH(OCH_3)_2$, m.p. 55–58°, b.p. 111°/11 mm., with intermediate formation of open ethylenoxy-compound. This acetal gives rise to the hydrochloride of β-aminolactic aldehyde, $NH_2CH_2CH(OH)CHO$, which, on oxidation, yields *iso*serine (p. 596) (Ber. **40**, 92).

A mixture of a little glyceraldehyde with dihydroxyacetone (see below) is formed by the oxidation of glycerol with dilute nitric acid, bromine or hydrogen peroxide in presence of a little ferrous sulphate (C. 1888, II. 104 : Ber. **33**, 3098). It is known as *glycerose*, and is condensed by sodium hydroxide to inactive *acrose*. This compound is related to dextrose, which can also be formed from each of the two separate compounds above mentioned.

αβ-Dihydroxybutyraldehyde, methylglyceraldehyde, $CH_3CH(OH)\cdot CH(OH)CHO$, is a syrupy body formed, analogously to glyceraldehyde, from its *acetal*, $CH_3CH(OH)CH(OH)CH(OC_2H_5)_2$, the oxidation product of crotonaldehyde acetal (Ber. **35**, 1914).

Pentaglycerol aldehyde, $CH_3C(CH_2OH)_2CHO$, is prepared by condensing propionaldehyde with two molecules of formaldehyde.

γ-Methyl-βγ-dihydroxy valeraldehyde, $(CH_3)_2C(OH)CH(OH)CH_2CHO$, is obtained by condensation of *d*-hydroxy*iso*butyric aldehyde with acetaldehyde (Monatsh. **22**, 443, 527).

Chloral aldol, $CCl_3\cdot CH(OH)\cdot CH(CHO)\cdot CHOH\cdot CH_3$, and *butyl chloral aldol*, $CH_3\cdot CHCl\cdot CCl_2\cdot CH(OH)\cdot CH(CHO)\cdot CHOH\cdot CH_3$, are thick oils. They result from the condensation of chloral or butyl chloral with paraldehyde and glacial acetic acid (Ber. **25**, 798).

αγ-Dihydroxycapraldehyde, see Ber. **56**, 759.

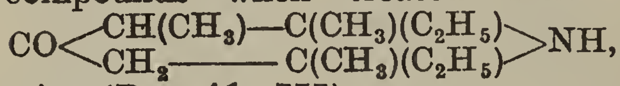
3. DIHYDROXYKETONES (OXETONES)

Dihydroxyacetone, *glycerol ketone* [propane diolone], $CH_2OH{\cdot}CO{\cdot}CH_2OH$, m.p. 68–75°, is prepared from its oxime by the action of bromine (p. 580). It tastes sweet and cooling. It is also obtained by heating glyceraldehyde with absolute pyridine (see p. 589, and Ber. **60,** 479).

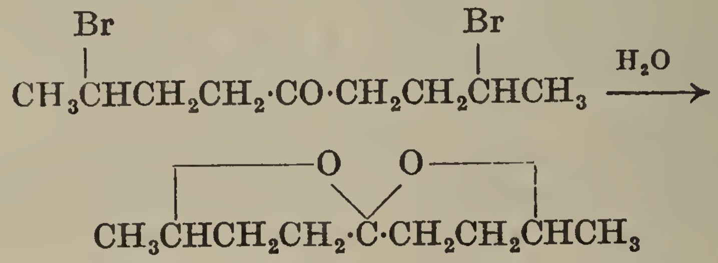
It occurs in dimolecular form which is depolymerized by distillation in high vacua (0·5 mm.) (Ber. **57,** 707). The monomolecular form is readily soluble in water, alcohol and acetone, but sparingly in ether. Reduction (p. 580) and the action of the sorbose bacterium (C. 1898, I. 985) convert it into glycerol (see also Glycerose, above). It reduces Fehling's solution in the cold. The *oxime*, $CH_2OH{\cdot}C(:NOH){\cdot}CH_2OH$, m.p. 84°, is produced from hydroxylamino-*tert.*-butylglycerol by HgO (Ber. **30,** 3161).

Chloroacetylcarbinol, $ClCH_2{\cdot}CO{\cdot}CH_2OH$, m.p. 74°, is formed from allene (p. 114) and HClO, together with some dichloroacetone (C. 1904, I. 576). *Diethoxyacetone,* $(C_2H_5O)CH_2{\cdot}CO{\cdot}CH_2(OC_2H_5)$, b.p. 195°, is prepared from αγ-diethoxyacetoacetic ester, and by distillation of calcium ethyl glycollate (Ber. **28,** R. 295). *Diaminoacetone,* $NH_2CH_2{\cdot}CO{\cdot}CH_2NH_2$, is obtained by the reduction of di*iso*nitrosoacetone (Ber. **28,** 1519). *ββ-Bromonitropropane-αγ-diol,* $HO{\cdot}CH_2{\cdot}CBr(NO_2){\cdot}CH_2OH$, m.p. 106°, is prepared from bromonitromethane and formaldehyde (C. 1899, I. 179).

Homologous Dihydroxyketones.—*Trimethyl triose,* $(CH_3)_2C(OH){\cdot}CH(OH)COCH_3$, b.p. 109°/19 mm., is obtained by the oxidation of mesityl oxide, $(CH_3)_2C:CHCOCH_3$ (p. 273), by permanganate, and appears to decompose rapidly into acetone and acetol. *Dihydroxymethylheptanone,* $(CH_3)_2C(OH)CH(OH)CH_2CH_2COCH_3$, m.p. 67°, is similarly prepared from methyl heptenone (p. 276) and permanganate (Ber. **34,** 2979: **35,** 1181). *γδ-Dihydroxybutyl methyl ketone,* $CH_2(OH)CH(OH)CH_2CH_2COCH_3$, b.p. 190°/22 mm., results from the splitting up of α-acetyl-δ-chloro-γ-valerolactone (the condensation product of epichlorohydrin and acetoacetic ester) by means of potassium carbonate (Ber. **34,** 1981). It is similarly prepared from epichlorohydrin and sodium acetylacetone (C. 1904, I. 356).

Derivatives of the unknown "*triacetone dialcohol,*" $Me_2C(OH){\cdot}CH_2{\cdot}CO{\cdot}CH_2{\cdot}CMe_2OH$, have been discussed under "phorone" (p. 273). Such are triacetonamine, triacetonediamine, etc. Methyl ethyl ketone forms similar compounds when treated with ammonia, *e.g.* *trimethyldiethylpiperidone,*  $CO\begin{matrix}\diagup CH(CH_3)\text{—}C(CH_3)(C_2H_5)\diagdown \\ \diagdown CH_2\text{———}C(CH_3)(C_2H_5)\diagup\end{matrix}NH$, m.p. 247°, corresponding with triacetonamine (Ber. **41,** 777).

The *oxetones,* discovered by *Fittig,* may be considered as the anhydrides of the γγ-dihydroxyketones. Their constitution is indicated by the formation of dimethyloxetone by treatment of the addition product of diallylacetone with two molecules of HBr with potash solution (*Volhard,* Ann. **267,** 90):



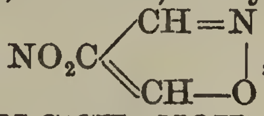
$$CH_3\overset{Br}{\overset{|}{C}}HCH_2CH_2{\cdot}CO{\cdot}CH_2CH_2\overset{Br}{\overset{|}{C}}HCH_3 \xrightarrow{H_2O}$$

The oxetones are obtained from the condensation products of the γ-lactones with sodium ethoxide by elimination of carbon dioxide (see p. 427).

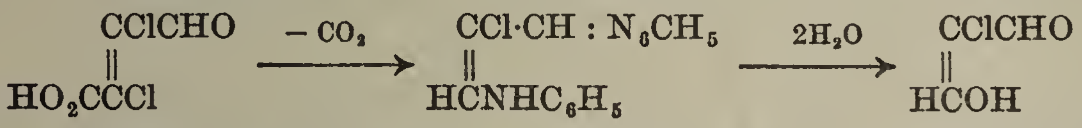
Oxetone, $C_7H_{12}O_2$, b.p. 159·4°. *Dimethyloxetone,* $C_9H_{16}O_2$, b.p. 169·5°, $D_0 = 0{\cdot}978$. *Diethyloxetone,* $C_{11}H_{20}O_2$, b.p. 209°. These oxetones are mobile liquids, and possess an agreeable odour. They are sparingly soluble in water, reduce an ammoniacal silver solution, and combine with 2HBr to γ-dibromoketones.

γ-Pyrone,  $CO<^{CH=CH}_{CH=CH}>O$ (Vol. III), may be considered the anhydride of an unsaturated dihydroxyketone.

4. HYDROXY-DIALDEHYDES

Nitromalonic dialdehyde, $NO_2CH(CHO)_2$, or $HO_2N : C(CHO)_2$, m.p. 50°, is a derivative of the dialdehyde of tartronic or hydroxymalonic acid. Its sodium salt is prepared from mucobromic acid (p. 457) and sodium nitrite (*cf.* C. 1900, II. 1262). The free aldehyde is obtained from the silver salt by hydrochloric acid, in ethereal solution. In aqueous solution it changes into formic acid and *sym.*-trinitrobenzene (Vol. II). It condenses with acetone in alkaline solution to form *p*-nitrophenol, and behaves similarly with a series of other ketones, ketonic acid esters, etc. (C. 1899, II. 609 : 1900, II. 560). Hydroxylamine converts nitromalonic aldehyde into nitro-isoxazole,  $NO_2C<^{CH=N}_{CH-O}$, and salts of the unstable *nitromalonic aldehyde dioxime*, $MO_2N{\cdot}C(CH : NOH)_2$, which can be converted into *nitromalonic aldoxime nitrile*, $NO_2HC(CN)CH : NOH$, and *fulminuric acid*, $NO_2HC(CN)CONH_2$ (p. 296) (C. 1903, I. 957).

Chloromalonic dialdehyde, $ClCH(CHO)_2$ or $CHO{\cdot}CCl : CHOH$, m.p. 144° (decomp.), and *bromomalonic dialdehyde*, $BrC_3H_3O_2$, m.p. 140° (decomp.), are prepared similarly to nitromalonic aldehyde from mucochloric and mucobromic acids. Aniline causes the loss of CO_2 from the acids, and converts them into dianils of the dialdehydes, which are liberated by hydrolysis :



$$\begin{matrix} CClCHO \\ \| \\ HO_2CCCl \end{matrix} \xrightarrow{-CO_2} \begin{matrix} CCl{\cdot}CH : N_6CH_5 \\ \| \\ HCNHC_6H_5 \end{matrix} \xrightarrow{2H_2O} \begin{matrix} CClCHO \\ \| \\ HCOH \end{matrix}$$

The two dialdehydes are also formed from ethoxyacrolein acetal $(C_2H_5O)CH : CH{\cdot}CH(OC_2H_5)_2$ (see Malonic dialdehyde, p. 399), by chlorine and bromine. The *enol*-configuration (see above) gives rise to strongly acid bodies giving a reddish-violet coloration with ferric chloride. Their stability towards alkalis is remarkable. Hydrazines give rise to pyrazoles (Ber. **37**, 4638).

5. HYDROXY-ALDEHYDE-KETONES

Hydroxypyroracemic aldehyde, $CHO{\cdot}CO{\cdot}CH_2OH$, is the simplest hydroxyaldehyde ketone. It is only known in the form of its *osazone*, m.p. 134°, which is produced by the interaction of phenylhydrazine and dihydroxyacetone (Ber. **28**, 1522).

Acetonetrisulphonic acid, $(SO_3H)_2CHCOCH_2(SO_3H)$, is a derivative of hydroxypyroracemic acid, prepared by the action of fuming sulphuric acid on acetone. It is decomposed by alkalis into methionic and sulphoacetic acid (C. 1902, I. 101).

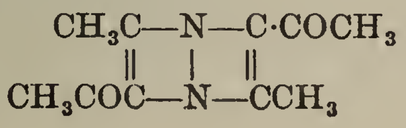
6. HYDROXY-DIKETONES

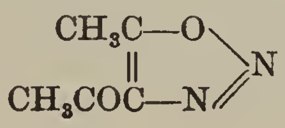
βγ-Diketobutyl alcohol, $CH_3CO{\cdot}COCH_2OH$, is the simplest hypothetical hydroxydiketone. A derivative is *α-dibromoethyl ketol*, $CH_3CBr_2{\cdot}CO{\cdot}CH_2OH$, m.p. 85°, prepared from bromotetrinic acid (p. 599) and bromine.

Derivatives of the *compound* $(CH_3)_2C(OH)COCOCH_3$ are found among the reaction products of nitrous or nitric acid on mesityl oxide oxime (p. 275).

α-Ethoxyacetylacetone, $(C_2H_5O)CH_2COCH_2COCH_3$, b.p. 84°/13 mm., is prepared from ethoxyacetic ester, sodium, and acetone (*cf.* p. 403) (C. 1907, I. 871).

γ-Aminoacetylacetone, $(CH_3CO)_2CHNH_2$, is formed when *iso*nitrosoacetyl acetone is reduced. Nitrous acid converts it into *dimethyldiacetylpyrazine* (1), m.p. 99°, and a diazo-anhydride or *furodiazole* (2), of which the connecting oxygen is easily replaceable by NR and S (see Vol. III ; pyrrodiazoles and thiodiazoles (Ann. **325**, 129) :

(1) 

(2) 

Hydroxymethyleneacetylactone, $(CH_3CO)_2C = CHOH$, m.p. 47°, b.p. 199°, which is the aci- or enol-form of formylacetylacetone, *formyldiacetylmethane,* $(CH_3CO)_2CH{\cdot}CHO$, is a stronger acid than acetic acid, and soluble in aqueous alkali acetates. It readily absorbs oxygen from the air, and is decomposed by gentle heating with water and HgO into CO_2 and acetylacetone; *copper salt,* m.p. 214°.

Ethoxymethyleneacetylactone, $(CH_3CO)_2C : CH(OC_2H_5)$, b.p. 141°/16 mm., is formed by condensation of acetylacetone with orthoformic ester by acetic anhydride. It decomposes with water into alcohol and the previous substance. It combines with acetyl acetone to form *methenyl-bis-acetylacetone,* $(CH_3CO)_2C{=}CH{-}CH(COCH_3)_2$, m.p. 118°, which is easily changed by ammonia into diacetyllutidine (Vol. III), and by abstraction of water into diacetyl *m*-cresol.

Aminomethyleneacetylacetone, $(CH_3CO)_2C : CHNH_2$, m.p. 144°, is formed from ethoxymethyleneacetylacetone and ammonia. *Anilinomethyleneacetylacetone,* $(CH_3CO)_2C : CHNHC_6H_5$, m.p. 90°, results when diphenyl formamidine, $C_6H_5N : CH{\cdot}NHC_6H_5$, is heated with acetylacetone (Ber. **35**, 2505).

7. DIALDEHYDE KETONES

Mesoxalic dialdehyde, $CHO{\cdot}CO{\cdot}CHO$, is formed, together with acetone peroxide, when phorone ozonide (p. 273), $(CH_3)_2C(O_3)CHCOCH(O_3)C(CH_3)_2$, is shaken with water, and the aqueous solution concentrated. It may be in the form of a syrup, the hydrate, solidifying to a glass-like substance, or a loose light yellow powder (a polymerized body), which, in aqueous solution, is strongly reducing in its action. The *diphenylhydrazone,* $CO[CH : NNHC_6H_5]_2$, m.p. 175° (decomp.), is formed by the action of phenylhydrazine, and also from acetone dicarboxylic acid (p. 623) and diazobenzene; *triphenylhydrazone,* $C_6H_5NHN : C[CH : NNHC_6H_5]_2$, m.p. 166° (Ber. **38**, 1634).

Dioxime, diisonitrosoacetone, $CO[CH : NOH]_2$, m.p. 144° (decomp.), is formed from acetone dicarboxylic acid and nitric acid; further action of N_2O_3 produces mesoxalic dialdehyde. The *trioxime,* $HON : C[CH : NOH]_2$, m.p. 171°, is formed by means of hydroxylamine (Ber. **38**, 1372).

8. ALDEHYDE DIKETONES

See above, under hydroxymethyleneacetylacetone or aci-formyldiacetylmethane (p. 592).

9. TRIKETONES

Triketones with adjacent CO groups are obtained from the 1 : 3-diketones by means of nitroso-dimethyl-aniline, followed by decomposition of the resulting *dimethylamino anil* by dilute sulphuric acid (Ber. **40**, 2714):

$$(CH_3CO)_2CH_2 \xrightarrow{NOC_6H_4N(CH_3)_2} (CH_3CO)_2C : NC_6H_4N(CH_3)_2 \xrightarrow{H_2O} (CH_3CO)_2CO.$$

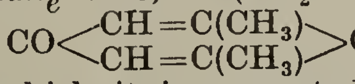
These triketones are orange-red oils which form colourless hydrates with water. They are very strongly reducing bodies.

Triketopentane, pentane-βγδ-trione, $CH_3CO{\cdot}CO{\cdot}CO{\cdot}CH_3$, b.p. 65–70°/30 mm., is formed by decomposing the reaction product of nitroso-dimethyl-aniline (Vol. II) and acetyl acetone. It is an *orange-yellow* oil, which unites with water to form a *colourless* crystalline *hydrate,* $C_5H_6O_3 + H_2O$. The *phenylhydrazone,* benzene azo-acetylacetone, $C_6H_5NHN : C(COCH_3)_2$, and the *oxime,* *iso*nitroso-acetylacetone, $HON : C(COCH_3)_2$, m.p. 75°, are prepared from sodium acetylacetone and diazobenzene salts or nitrous acid (Ann. **325**, 139, 193). Triketopentane and phenylhydrazine form a *bis-phenylhydrazone*; with semicarbazide a *bis-semicarbazone,* m.p. 221°; with hydrazine hydrate, *dimethyl-hydroxy-pyrazole* (*cf.* 1 : 3-diketones, p. 409); with *o*-phenylene diamine, a *quinoxaline*-derivative (*cf.* 1 : 2-diketones, p. 401). Alkalis decompose triketopentane into 2 molecules of acetic acid and formaldehyde.

βγδ-Triketohexane, $CH_3CO{\cdot}CO{\cdot}COC_2H_5$, b.p. 70°/18 mm., is obtained, analogously to triketopentane, from acetyl methyl ethyl ketone, $CH_3COCH_2{\cdot}COC_2H_5$ (Ber. **40**, 2728).

βγε-Triketohexane. The *trioxime,* $CH_3C(NOH)CH_2C(NOH)C(NOH)CH_3$, m.p.

159°, is formed, similarly to succinic dialdoxime from pyrrole (p. 408), from β-nitroso-αα-dimethyl-pyrrole and hydroxylamine (C. 1908, I. 1630).

Diacetylacetone, βδζ-triketoheptane, βδζ-heptan$_e$trione, $CO(CH_2COCH_3)_2$, m.p. 49°, is produced from 2:6-dimethyl pyrone,  $CO{<}{\genfrac{}{}{0pt}{}{CH{=}C(CH_3)}{CH{=}C(CH_3)}}{>}O$, and concentrated barium hydroxide solution, from which it is separated by hydrochloric acid. It decomposes spontaneously into water and dimethyl pyrone (Ann. **257**, 276). Ferric chloride produces a deep-red colour with it. The *oxime*, m.p. 68°, easily turns into an anhydride (Ber. **28**, 1817). With sodium and iodomethane it is converted into a *dimethyldiacetylacetone*, m.p. 87° (C. 1900, II. 625).

Acetonylacetylacetone, γ-acetylhexane-βε-dione, $CH_3COCH_2{\cdot}CH(COCH_3)_2$, b.p. 156°/35 mm., is formed from sodium acetylacetone and chloroacetone (C. 1902, II. 346).

10. DIHYDROXY-MONOCARBOXYLIC ACIDS

The acids of this series bear the same relation to the glycerols that the lactic acids sustain to the glycols, and may also be looked on as being dihydroxy-derivatives of the fatty acids. They may be artificially prepared by means of the general methods used in the production of hydroxy-acids, and also by the oxidation of unsaturated acids with potassium permanganate (p. 341) (Ber. **21**, R. 660 : Ann. **283**, 109).

Glyceric acid, *dihydroxypropionic acid*, $CH_2OH{\cdot}CHOH{\cdot}COOH$, is formed : (1) By the careful oxidation of glycerol with nitric acid (method of preparation, Ber. **9**, 1902 : **10**, 267 : **15**, 2071) ; or by oxidizing glycerol with mercuric oxide and barium hydroxide solution (Ber. **18**, 3357 : **55**, 1406), or with silver chloride and sodium hydroxide (Ber. **29**, R. 545), or with red lead and nitric acid (C. 1898, I. 26). The calcium salt is decomposed with oxalic acid (Ber. **24**, R. 653) :

$$CH_2(OH){\cdot}CH(OH){\cdot}CH_2{\cdot}OH + O_2 = CH_2(OH){\cdot}CH(OH){\cdot}CO{\cdot}OH + H_2O.$$

(2) By the action of silver oxide on β-chlorolactic acid, $CH_2Cl{\cdot}CH(OH){\cdot}CO_2H$, and α-chlorohydracrylic acid, $CH_2(OH){\cdot}CHCl{\cdot}CO_2H$ (p. 421). (3) By heating glycidic acid with water (p. 594).

Glyceric acid forms a syrup which cannot be crystallized. It is easily soluble in water, alcohol, and acetone. It is optically inactive, but as it contains an asymmetric carbon atom (p. 37), it may be changed to active *lævorotatory* glyceric acid by the fermentation of its ammonium salt, through the agency of *Penicillium glaucum. Bacillus ethaceticus*, on the other hand, decomposes inactive glyceric acid so that the *lævorotatory* glyceric acid is destroyed and the *dextrorotatory* acid remains (Ber. **24**, R. 635, 673). This glyceric acid is also formed by reduction of hydroxypyroracemic acid (p. 598), whilst the *lævorotatory* glyceric acid is obtained by the action of milk of lime on glycuronic acid. Further, both forms can be separated by means of brucine (Ber. **37**, 339 : C. 1905, I. 1085, 1089).

Stereochemical Relationships.—*d*-Glyceraldehyde can be oxidized by mercuric oxide and sodium hydroxide to *lævorotatory* (−)-glyceric acid. This (−)-glyceric acid is therefore *d*-glyceric acid (Ber. **55**, 1404).

Reactions.—When the acid is heated above 140° it decomposes into water, pyroracemic and pyrotartaric acids. When fused with potassium hydroxide it forms acetic and formic acids, and when boiled with it, yields oxalic and lactic acids. Phosphorus iodide converts it into β-iodopropionic acid. Heated with hydrochloric acid, it yields α-chlorohydracrylic acid and αβ-dichloropropionic acid. (See also β-chlorolactic acid (p. 421).)

When glyceric acid is kept, it forms an anhydride probably analogous to lactide. This is sparingly soluble in water, and crystallizes in fine needles.

Salts and Esters.—Its *calcium salt,* $(C_3H_5O_4)_2Ca + 2H_2O$, dissolves readily in water; *lead salt,* $(C_3H_5O_4)_2Pb$, is sparingly soluble in cold water.

Ethyl ester is formed on heating glyceric acid with absolute alcohol. The rotatory power of the optically active glyceric esters increases with the molecular weight (Ber. **26**, R. 540), and attains its maximum with the butyl ester (Ber. **27**, R. 137, 138: C. 1897, I. 970).

The *homologues of glyceric acid* have been obtained (1) from the corresponding dibromo-fatty acids; (2) from the corresponding glycidic acids on heating them with water (Ann. **234**, 197); and (3) by oxidizing the corresponding unsaturated carboxylic acids (p. 341) with potassium permanganate or persulphuric acid, which at the same time occasion stereoisomeric transformation (*cf.* Dihydroxystearic acid) (Ann. **268**, 8: Ber. **22**, R. 743: C. 1903, I. 319).

αβ-Dihydroxybutyric acid, β-methylglyceric acid, $CH_3CH(OH)CH(OH)CO_2H$, m.p. 75°, is resolved into its optically active components by quinidine. Also, the (+)-form appears to result from oxycellulose by the action of milk of lime (Ber. **32**, 2598: C. 1904, I. 933). *αβ-Dihydroxy*iso*butyric acid, α-methylglyceric acid,* $CH_2OH{\cdot}C(CH_3)(OH)CO_2H$, m.p. 100°.

Tiglyceric acid, m.p. 88°, and *anglyceric acid,* m.p. 111°, are the oxidation products of tiglic acid and angelic acid (Ann. **283**, 109). *α-Ethylglyceric acid,* m.p. 99°. *α-Propylglyceric acid,* m.p. 94°. *α-*iso*Propylglyceric acid,* m.p. 102° (C. 1899, I. 1071). *α-Ethyl-β-methylglyceric acid,* $CH_3CH(OH)C(C_2H_5)(OH)COOH$, m.p. 145°, is formed from α-ethylcrotonic acid (Ann. **334**, 68).

*αβ-Dihydroxy*iso*octylic acid,* $(CH_3)_2CHCH_2CH_2CH(OH)CH(OH)CO_2H$, m.p. 106° (Ann. **283**, 291).

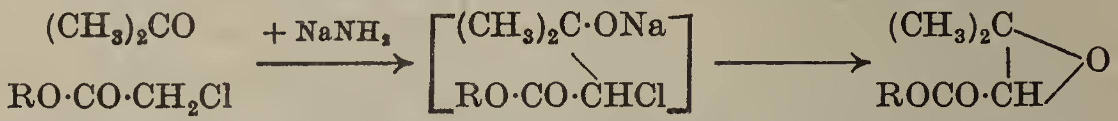
α-iso*Propyl-β-*iso*butylglyceric acid,* m.p. 154° (Ber. **29**, 508).

βγ-Dihydroxybutyric acid, butylglyceric acid, $CH_2(OH){\cdot}CH(OH)CH_2CO_2H$, is a thick oil. The βγ-dihalogen and hydroxy-halogen-butyric acids corresponding with these, are obtained from vinylacetic acid (p. 345), or from epihalogenohydrins (p. 587), and hydrocyanic acid. *γ-Ethoxy-β-hydroxybutyric acid* is a syrup; *ethyl ester,* b.p. 121°/13 mm.; *nitrile,* b.p. 245°, is prepared from epiethylin (p. 588) and hydrocyanic acid (C. 1903, II. 106: 1905, I. 1586).

γδ-Dihydroxyvaleric acid, $CH_2(OH)CH(OH)CH_2CH_2CO_2H$, rapidly decomposes into water and forms a hydroxylactone.

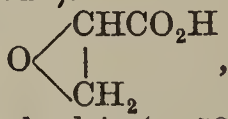
Dihydroxyundecoic acid, $C_{11}H_{22}(OH)_2O_2$, m.p. 85°, is prepared from undecylenic acid (p. 348). *Dihydroxystearic acids,* $C_{18}H_{34}(OH)_2O_2$ (see Oleic and Elaidic acids, p. 349) (C. 1902, I. 179: 1903, I. 319). *Dihydroxybehenic acid,* $C_{22}H_{42}(OH)_2O_2$, m.p. 127°, is formed from erucic acid, $C_{22}H_{42}O_2$.

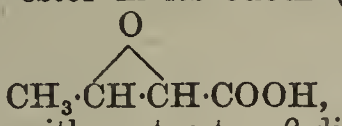
Glycidic acids are formed (1) by the action of alcoholic potassium hydroxide on the addition product of hypochlorous acid and olefinecarboxylic acid (Ann. **266**, 204); (2) by condensation of ketones and α-halogen fatty esters by sodium ethoxide or sodium amide, whereby the glycidic esters are formed:

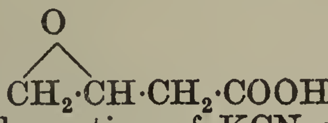


The acids obtained from these esters easily lose CO_2 and change into aldehydes or ketones (C. 1906, I. 669: Ber. **38**, 699).

In general, the glycidic acids, like ethylene oxide, form addition products with the halogen acids, water and ammonia, whereby chloro-hydroxy fatty acids, dihydroxy, and amino-hydroxy-fatty acids can be prepared. Many add sodium malonic ester, etc. (C. 1906, II. 421).

Glycidic acid, epihydrinic acid, , is isomeric with pyroracemic acid. It is produced, like epichlorohydrin (p. 587), from α-chlorohydracrylic acid and β-chlorolactic acid by means of alcoholic potassium hydroxide. Glycidic acid, separated from its salts by means of sulphuric acid, is a mobile liquid miscible with water, alcohol, and ether. It is very volatile and has a penetrating odour. The free acid and its salts are not coloured red by iron sulphate solutions (distinction from isomeric pyroracemic acid). It combines with the halogen acids to β-halogen lactic acids, and with water, either on boiling or on standing, it yields glyceric acid. Its *ethyl ester*, m.p. 162°, obtained from the silver salt with ethyl iodide, resembles malonic ester in its odour (Ber. **21**, 2053).

β-Methylglycidic acid,  $CH_3\cdot\overset{O}{CH\cdot CH}\cdot COOH$, is known in two modifications. The one, m.p. 84°, unites with water to αβ-dihydroxybutyric acid. The other modification is a liquid.

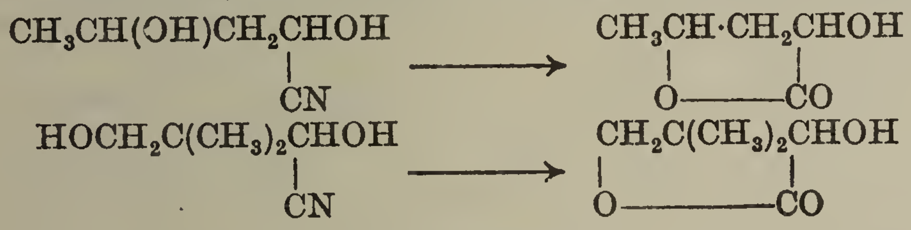
Epihydrincarboxylic acid,  $\overset{O}{CH_2\cdot CH}\cdot CH_2\cdot COOH$, m.p. 225°, is obtained from its nitrile, which results from the action of KCN on epichlorohydrin (p. 587).

α-Methylglycidic acid consists of shining leaflets. The *ethyl ester*, b.p. 162–164° (Ber. **21**, 2054).

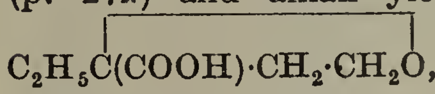
αβ-Dimethylglycidic acid, m.p. 62° (Ann. **257**, 128).

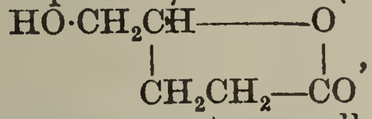
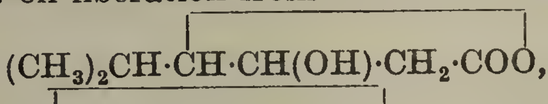
ββ-Dimethylglycidic acid is formed as a syrup from α-chloro-β-hydroxy-*iso*valeric acid (Ann. **292**, 282); *ethyl ester*, b.p. 181°, is obtained in good yield from acetone, chloroacetic ester and sodium amide (see above) (Ber. **38**, 707). *ββ-methylethylglycidic ester*, b.p. 198°; *ββ-diethylglycidic ester*, b.p. 212°; and *ββ-trimethylglycidic ester*, b.p. 81°/20 mm., etc., are formed according to method 2.

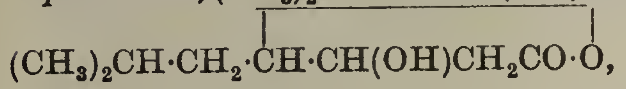
Hydroxylactones are formed from those dihydroxy-acids in which the hydroxyl group stands in the γ-position to the carboxyl group. Thus, α-hydroxy-γ-lactones are obtained by hydrolysis of cyanohydrins of the aldols (p. 390):



These hydroxylactones are readily caused by acids to undergo isomeric transformation accompanied by wandering of the OH-group; in the case of α-hydroxyvalerolactone (see above), the OH-group apparently migrates first to the β- and finally to the γ-position, forming lævulinic acid (p. 477) (Ann. **334**, 68: C. 1904, I. 217). On the other hand, the cyanohydrin of β-chloro-diethyl-ketone (p. 272) and alkali yield salts of *ethyltrimethylene oxide carboxylic acid*:


$C_2H_5C(COOH)\cdot CH_2\cdot CH_2O$, b.p. 136°/16 mm. (C. 1908, I. 1615).

δ-Hydroxyvalerolactone,  $\begin{matrix} HO\cdot CH_2CH & — & O \\ | & & | \\ CH_2CH_2 & — & CO \end{matrix}$, b.p. 300–301°, results from the action of potassium permanganate on allyl acetic acid (Ann. **268**, 61). *Hydroxycaprolactone* and *hydroxy*iso*caprolactone*, $C_6H_{10}O_3$, are colourless liquids, into which the oxidation products of hydrosorbic acid by means of $KMnO_4$ rapidly pass on liberation from their barium salts (Ann. **268**, 34). *Hydroxy*iso-*heptolactone*,  $(CH_3)_2CH\cdot CH\cdot CH(OH)\cdot CH_2\cdot COO$, m.p. 112°. *Hydroxy*iso*octolactone*,


$(CH_3)_2CH\cdot CH_2\cdot CH\cdot CH(OH)CH_2CO\cdot O$, m.p. 33° (Ann. **283**, 278, 291).

Monoamino-hydroxy-carboxylic Acids

The following sections containing the hydroxy-amino, thio-amino, and diamino-carboxylic acids embrace a number of substances which, with the simple amino-acids (pp. 434–445), command the greatest interest, as constituting the decomposition products of the proteins—serine, cystine, ornithine, arginine, proline, lysine.

α-Aminohydracrylic acid, α-amino-β-hydroxy-propionic acid, $HO\cdot CH_2CH(NH_2)COOH$, m.p. 246° (decomp.), has been named **serine**, because it was first obtained from sericin (silk-gum). It is also obtained from silk-fibroin, horn, gelatin, casein, etc., by hydrolysis with dilute acids. It was first synthesized from glycolyl aldehyde (p. 389), ammonia, hydrocyanic acid, and hydrochloric acid (Ber. **35**, 3794); also, by the following steps: formic ester and hippuric ester were condensed by sodium ethoxide to formylhippuric ester, $CHO{\cdot}CH(NHCOC_6H_5)COOC_2H_5$ (p. 599), which, on reduction, yields *benzoylserine ester*, $HOCH_2CH(NHCOC_6H_5)COOC_2H_5$, m.p. 80°; this, on hydrolysis, gives serine (Ann. **337**, 222). The best synthesis consists in preparing *β-ethoxy-α-amino-propionic acid*, $C_2H_5OCH_2{\cdot}CH(NH_2)COOH$, m.p. 256° (decomp.), from ethoxy-acetaldehyde (p. 390), NH_3, HCN, and HCl, and decomposing this with hydrobromic acid (Ber. **39**, 2644).

Serine forms hard crystals, soluble in 24 parts of water at 20°, but insoluble in alcohol and ether. As an amino-acid it reacts neutral, but forms salts with bases and acids. The taste is sweet, like glycocoll.

Both synthetic and natural serine are optically inactive on account of racemization; resolution can be effected through the *quinine salts* of the p-*nitrobenzoyl*-derivative into d- and l-*serine*, $[\alpha]_D^{20} = \pm 6{\cdot}8°$, m.p. 228° (decomp.), soluble in 3–4 parts of water. *d*-Serine tastes sweeter than *l*-serine (Ber. **38**, 2942).

Serine methyl ester, a syrup, loses alcohol spontaneously and passes into a diketo-piperazine (p. 446):

$$\mathrm{CH_2OH{\cdot}CH}<\begin{matrix}\mathrm{NH{\cdot}CO}\\\mathrm{CO{\cdot}NH}\end{matrix}>\mathrm{CHCH_2OH}$$

of which the *l*-form $[\alpha]_D^{25} = -67{\cdot}46°$ appears to be identical with a decomposition product of silk-fibroin.

Nitrous acid converts serine into glyceric acid. PCl_5 changes serine ester into β-chloro-α-amino-propionic acid, which, on reduction, yields alanine; *l*-serine gives *l*-(+)-alanine (p. 443).

β-Naphthalenesulphoserine, m.p. 214°. *Serine phenyl isocyanate compound*, m.p. 169°.

β-Amino-lactic acid, *α-hydroxy-β-aminopropionic acid*, iso*serine*, $H_2NCH_2{\cdot}CH(OH)COOH$, m.p. 248° (decomp.), is prepared from β-chlorolactic acid (p. 421) or from glycidic acid (p. 594), and NH_3; from αβ-diaminopropionic acid, hydrochloride, and silver nitrite (Ber. **37**, 336, 343, 1278); also by reduction of the addition product of acrylic acid and nitrous acid (C. 1903, II. 343); iso*serine ethyl ester*, m.p. 78°; *methyl ester*, a syrup, passes easily into the dipeptide iso*seryl* iso*serine ester*. *iso*Serine ester hydrochloride yields glyceric ester with sodium nitrite. Reduction produces β-alanine (p. 448) (Ber. **37**, 1277: **38**, 4171).

α-Amino-β-hydroxybutyric acid, $CH_3CH(OH){\cdot}CH(NH_2)COOH$, m.p. 230° (decomp.), is obtained by reduction of the addition product of crotonic acid and nitrous acid. HI and phosphorus yield α-aminobutyric acid (C. 1903, II. 554).

α-Amino-γ-hydroxybutyric acid, $HOCH_2{\cdot}CH_2CH(NH_2)COOH$, m.p. 207° (indefinite), is obtained by the decomposition of β-hydroxy-ethyl-phthalimidomalonic mono-ester lactone, a product of ethylene bromide and sodium phthalimidomalonic ester (C. 1908, II. 683). The hydrobromide of the lactone (formula, see below) is obtained by heating together hydrobromic acid and *γ-phenoxy-α-aminobutyric acid*, m.p. 233° (decomp.). This substance is prepared by acting with ammonia on phenoxybromobutyric acid, the result of brominating and then decomposing phenoxyethylmalonic acid. The oily lactone changes spontaneously into *di-β-hydroxyethyldiketopiperazine*, m.p. 192° (Ber. **40**, 106):

$$2\,\overline{\mathrm{OCH_2CH_2CH}}<\begin{matrix}\mathrm{CO}\\\mathrm{NH_2}\end{matrix} \longrightarrow \mathrm{HOCH_2CH_2CH}<\begin{matrix}\mathrm{CO{\cdot}NH}\\\mathrm{NH{\cdot}CO}\end{matrix}>\mathrm{CH{\cdot}CH_2CH_2OH}.$$

α-Amino-γ-hydroxyvaleric acid, $CH_3CH(OH)CH_2CH(NH_2)COOH$, m.p. 212° with decomposition, is prepared from aldol, NH_3, HCN, and HCl. Like the previous substance, it readily passes into the *aminolactone*, b.p. 124°/13 mm., which spontaneously changes into the *dipeptide anhydride*, m.p. 224°. Reduction with HI yields α-amino-*n*-valeric acid (Ber. **35**, 3797).

δ-Amino-γ-hydroxyvaleric acid, $NH_2CH_2CH(OH)CH_2CH_2COOH$, is formed from allylacetic acid dibromide (Ber. **32**, 2682).

α-Amino-δ-hydroxyvaleric acid, $HOCH_2{\cdot}CH_2CH_2CH(NH_2)COOH$, m.p. 224° (decomp.), is prepared from phthalimidobromopropylmalonic ester, $BrCH_2CH_2{\cdot}CH_2C(CO_2R)_2N(CO)_2C_6H_4$ (C. 1905, II. 398).

Aminothiolcarboxylic Acids

Cysteine, $HS \cdot CH_2 \cdot CH(NH_2) \cdot COOH$, the sulphur analogue of serine, very readily passes by oxidation in the air to disulphide *cystine* $(\cdot S \cdot CH_2 \cdot CH(NH_2) \cdot COOH)_2$. A derivative of cysteine of physiological importance is the tripeptide **glutathione**, first isolated by Hopkins in 1921 (Biochem. J. **15**, 286). It is of importance in many cellular oxidation processes. It was at first regarded as a dipeptide of cystine and glutamic acid, but more recent work (J. Biol. Chem. **72**, 147 : **84**, 269 : **87**, 55 : **88**, 409) shows that it is a tripeptide containing glycine, of the constitution

$$\underbrace{HOCO \cdot CH(NH_2) \cdot CH_2 \cdot CH_2 \cdot CO}_{\text{Glutamic acid.}} \cdot \underbrace{NH \cdot CH(CH_2 \cdot SH) \cdot CO}_{\text{Cysteine.}} \cdot \underbrace{NH \cdot CH_2 \cdot COOH}_{\text{Glycine.}}$$

The *disulphide*, **cystine**, $HOOC \cdot CH(NH_2)CH_2S \cdot SCH_2CH(NH_2)COOH$, decomposes at 258–261°. The *lævorotatory* form of this substance is obtained from many proteins, especially from hair, horn, egg-shells. It is the chief sulphur compound of the proteins. It occurs also in the calculi of patients with cystinuria (C. 1905, II. 1237). Cystine and cysteine yield a black precipitate of PbS with lead acetate solution and give a purple colour with sodium nitroprusside and alkali. The action of nitrous and hydrochloric acids changes cystine into α-chlorodithiolactic acid, $(SCH_2CHCl \cdot COOH)_2$, which yields β-dithiopropionic acid, $(SCH_2CH_2COOH)_2$, on reduction. Bromine water oxidizes it to cysteinic acid, $SO_3H \cdot CH_2CH(NH_2)COOH$, which loses CO_2 and changes into taurine, $SO_3H \cdot CH_2CH_2NH_2$ (p. 376) (C. 1902, II. 1360).

Cysteine and cystine are closely connected with serine : (1) when β-chloro-α-aminopropionic acid (above) is heated with $Ba(SH)_2$, it yields first cysteine and then cystine ; (2) the synthetic benzoyl serine ester (p. 596), treated with P_2S_5 gives benzoyl cysteine ester, $HSCH_2CH(NHCOC_2H_5)COOC_2H_5$, m.p. 158°, which on hydrolysis is changed to *i*-cysteine and *i*-cystine (Ann. **337**, 222 : Ber. **40**, 3717). *l*-Serine produces the natural *lævorotatory* cystine $[\alpha]^{20}_{D} = -224°$. Cystine forms crystals which dissolve with difficulty in water.

Salts (C. 1905, II. 220) ; *dimethyl ester* is a syrup ; *hydrochloride*, m.p. 173° (decomp.) (C. 1905, II. 1237).

α-Thio-β-aminopropionic acid, iso*cysteine*, $NH_2CH_2CH(SH)COOH$, *hydrochloride*, m.p. 141° (decomp.), is obtained from β-alanine (p. 448) by transformation of the ureide, hydrouracil (p. 501)—into bromohydrouracil, this into thiocyanohydrouracil, and the decomposition of the latter with hydrochloric acid:

$$\begin{array}{l} CO\text{——}NH \cdot CH_2 \\ | \qquad\quad\;\; | \\ NH\text{—}CO\text{—}CH \cdot SCN \end{array} \longrightarrow \begin{array}{l} NH_2CH_2 \\ \qquad\;\; | \\ COOH \cdot CH \cdot SH \end{array}.$$

*iso*Cysteine is oxidized by iodine to iso*cystine*, $[SCH(CH_2NH_2)COOH]_2$, m.p. 155° (decomp.) ; and by bromine water into iso*cysteinic* acid, $HO_3S \cdot CH(CH_2NH_2) \cdot COOH$ (Ber. **38**, 630).

α-Thio-γ-aminobutyric acid and *γ-amino-α-butyrosulphonic acid*, $NH_2CH_2 \cdot CH_2CH(SO_3H)COOH$ (Ber. **41**, 513).

γ-Methylthiol-α-aminobutyric acid, **Methionine**, $MeS \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH$, is an amino acid isolated from casein by Mueller in 1923 (J. Biol. Chem. **56**, 157) : it has m.p. 281° and $[\alpha]^{20}_{D} - 7 \cdot 2°$ (probably partly racemized) : it has recently been synthesized by Barger and Coyne (Biochem. J. **22**, 1417).

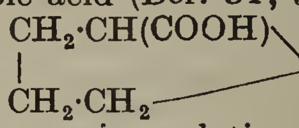
Diaminomonocarboxylic Acids

Diaminopropionic acid, $CH_2NH_2 \cdot CHNH_2 \cdot CO_2H$, is obtained from αβ-dibromopropionic acid by means of aqueous ammonia ; also by the decomposition of hippuryl aspartic acid (p. 610). Optical resolution has been performed by means of its salts with *d*-camphorsulphonic acid (Vol. II) ; and through the quinidine salts of dibenzoyldiaminopropionic acid (C. 1906, II. 1119 : Ber. **39**, 2950). The *dextrorotatory* (*hydrochloride*, $[\alpha]_D + 25 \cdot 09°$, m.p. 245° (decomp.) Ber. **40**, 1068) compound reacts with 1 molecule of HNO_2 to form *iso*serine (p. 596), and with 2 molecules of HNO_2 to produce *l*-glyceric acid. *Diaminopropionic methyl ester* is changed by heat into the ester of diaminopropionyldiaminopropionic acid, one of the dipeptides (Ber. **38**, 4173).

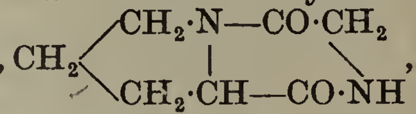
αβ-Diaminobutyric acid, $CH_3CH(NH_2) \cdot CH(NH_2)COOH$, is formed from αβ-dibromobutyric acid and ammonia, together with a hydroxyaminobutyric acid (C. 1906, II. 764).

αγ-Diaminobutyric acid, $NH_2CH_2CH_2CH(NH_2)COOH$, is obtained from phthalimidoethylmalonic ester by bromination, hydrolysis of the phthalimido-α-bromobutyric acid formed, treatment with NH_3, and final decomposition; *dibenzoyl* derivative, m.p. 201° (Ber. **34**, 2900).

αδ-Diaminovaleric acid, $NH_2CH_2CH_2CH_2CH(NH_2)COOH$, is synthetically prepared from δ-phthalimido-α-bromovaleric acid, and from the condensation product of phthalimidopropyl bromide with sodium phthalimidomalonic ester (C. 1903, II. 34). It is the optically inactive form of the dextrorotatory *ornithine*. This body is produced, together with urea by the action of barium hydroxide solution, on **arginine**, *α-amino-δ-guanidinovaleric acid*, $NH_2(NH)C{\cdot}NHCH_2CH_2CH_2CH(NH_2)COOH$, a substance found among the decomposition products of many animal and vegetable proteins (Ber. **34**, 3236 : **38**, 4187). (Conversion of arginine into ornithine, see Z. physiol. Chem. **159**, 179.) Permanganate converts arginine into γ-guanidinobutyric acid (C. 1902, II. 200). It is prepared synthetically from cyanamide, $CN{\cdot}NH_2$, and ornithine (Ber. **34**, 454 : C. 1902, I. 300). The *dibenzoyl* derivative of ornithine, *ornithuric acid*, m.p. 185°, occurs in the urine of hens when fed with benzoic acid (Ber. **31**, 3183).

α-Pyrrolidinecarboxylic acid, **proline**,  $\begin{matrix}CH_2{\cdot}CH(COOH)\\ |\\ CH_2{\cdot}CH_2\end{matrix}\!\!>NH$, is the *imine* of αδ-diaminovaleric acid. It results when casein, gelatin, and other proteins are treated with hydrochloric acid. It is related to the *coca*-alkaloids (Vol. III). It can be synthetically prepared in several ways, more particularly from αδ-dibromovaleric acid and ammonia; and from δ-bromo-α-aminovaleric acid, the decomposition product of bromopropyl phthalimidomalonic ester (C. 1908, II. 680 : Ber. **33**, 1160 : **34**, 458 : **37**, 3071 : C. 1902, II. 284).

αε-Diaminocaproic acid, $NH_2CH_2CH_2CH_2CH_2CH(NH_2)COOH$, is prepared synthetically by the reduction of α-hydroximido-γ-cyanovaleric acid by means of sodium and alcohol. This product is the inactive form of the optically active **lysine**, which is formed in the decomposition of casein and other proteins. Pancreatic decomposition converts lysine into pentamethylene diamine (cadaverine, p. 384); and ornithine into tetramethylene diamine (putrescine, p. 385) (Ber. **32**, 3542 : C. 1902, I. 985). Permanganate oxidizes lysine into glutaric acid, together with hydrocyanic and oxalic acids (Ber. **35**, 3401).

Like the simple amino-acids, the hydroxyamino-, thioamino-, and diaminocarboxylic acids are connected with one another and with the mono-amino acids in so far that through their amides they go to form protein-like bodies, such as di- and poly-peptides and dipeptide anhydrides (diketopiperazines, p. 446). Therefore, in general, similar methods of formation can be employed in both cases: diglycylcystine, $[NH_2CH_2CONHCH(COOH)CH_2S]_2$, is prepared from bis-chloroacetyl cystine and ammonia; *leucylproline*, from bromo*iso*caproyl proline; *anhydride*, m.p. 126–129°. *Prolylalanine*, from αδ-dibromovalerylalanine; *anhydride*, m.p. 171–121°. *Prolylglycine anhydride*,  $CH_2\!<\!\begin{matrix}CH_2{\cdot}N{-}CO{\cdot}CH_2\\ |\qquad\quad \backslash\\ CH_2{\cdot}CH{-}CO{\cdot}NH\end{matrix}$, m.p. 183°, is obtained by tryptic digestion of gelatin (*cf.* Ber. **37**, 3071, 4575 : **38**, 4173 : **39**, 2060, etc.).

Dihydroxyolefine Monocarboxylic Acids

The γ-lactones of these bodies are the tetronic acid and mono-alkyl tetronic acids. These substances can also be looked on as being the aci-forms of β-keto-γ-lactones. They are, therefore, considered under the heading of hydroxyketone-carboxylic acids (below) according to the principle set down on p. 453.

11, 12. ALDO-HYDROXY-CARBOXYLIC ACIDS AND HYDROXY-KETO-CARBOXYLIC ACIDS

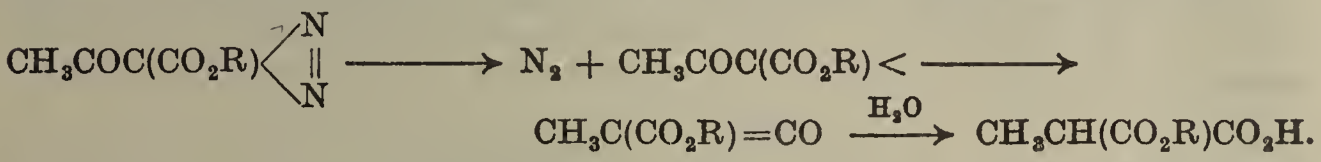
Hydroxypyroracemic acid, $CH_2OH{\cdot}CO{\cdot}COOH$, or *tartronic acid semi-aldehyde*, $CHO{\cdot}CH(OH)COOH$, is formed when nitrocellulose (collodion cotton) is treated with sodium hydroxide solution. Reduction converts it into (+)-glyceric acid; hydrocyanic and hydrochloric acids produce *l*- and some meso-tartaric acid (C.

1905, I. 1088). *Formyl-* or *hydroxymethylene hippuric ester*, $OCH{\cdot}CH(NHCOC_6H_5)CO_2R$, or $HOCH : C(NHCOC_6H_5)CO_2R$, m.p. 128° (*cf.* p. 596). *Tribromomethyl ketol*, $CH_2OH{\cdot}CO{\cdot}CBr_3$, decomposes at 174° (see Bromotetronic acid, below).

The following substances are derived from α-hydroxyacetoacetic acid, $CH_3COCH(OH)COOH$, and γ-hydroxyacetoacetic acid, $HOCH_2{\cdot}COCH_2COOH$, or from their enols both of which are unknown in the simple form.

α-*Thioacetoacetic ester*, $S[CH(COCH_3)CO_2C_2H_5]_2$, *keto*-form, m.p. 76°, is prepared by the action of sulphur chloride or thionyl chloride on acetoacetic ester. The solid *keto*-form is converted into the oily *enol*-form by the influence of solvents (alcohol, benzene), or a trace of alkali; soda causes the re-production of the keto-body (Ber. **39**, 3255). *Benzene-sulphonyl-thioacetoacetic ester*, $C_6H_5{\cdot}SO_2{\cdot}SCH(COCH_3)CO_2C_2H_5$, m.p. 55°, is prepared from α-chloroacetoacetic ester and benzene thiosulphonate (J. pr. Chem. [2] **70**, 375).

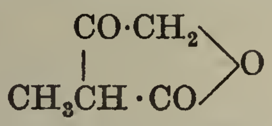
α-*Aminoacetoacetic acid*, $CH_3CO{\cdot}CH(NH_2)COOC_2H_5$, is obtained by the reduction of *iso*nitrosoacetoacetic ester (p. 602) by zinc and sulphuric acid, together with dimethylpyrazinedicarboxylic ester (Vol. II). Aminoacetoacetic ester reacts with nitrous acid to form *diazoacetoacetic ester*, $CH_3{\cdot}CO{\cdot}C(:N_2){\cdot}CO_2Et$, an oil, b.p. 102–104°/12 mm. Alkalis convert it into acetic and diazoacetic acids (p. 458). When boiled with water or superheated to above 110°, it breaks down into nitrogen and methylmalonic mono-ester (*L. Wolff*, Ann. **325**, 129), a decomposition which may be explained as follows (*Schroeter*):



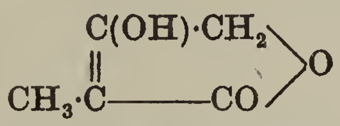
Ammonia or amines convert the diazo-anhydride into triazoles: H_2S produces thiodiazoles (Vol. III). β-Diketones react with it as with aromatic diazo-bodies (Vol. II), forming azo-compounds, such as hydrazones, which easily condense further to pyrazoles.

Lactones of the γ-hydroxyacetoacetic acids (pp. 476, above) are tetronic acid and the alkyl tetronic acids. Substances of this class were obtained by *Demarçay* from γ-mono-bromo-substituted mono-alkyl acetoacetic esters by alcoholic potassium hydroxide, and were named by him tetrinic acid, pentinic acid, etc. *Michael* recognized in tetrinic acid a keto-lactone (formula 1). *L. Wolff* examined the parent substance of these compounds and called it tetronic acid, and derived *Demarçay's* acids from it under the names of α-methyl-, α-ethyl tetronic acid, etc. (Ann. **291**, 226). The keto- and enol-formulæ (A and B) are applicable to tetronic acid and α-methyltetronic acid (tetrinic acid):

A.

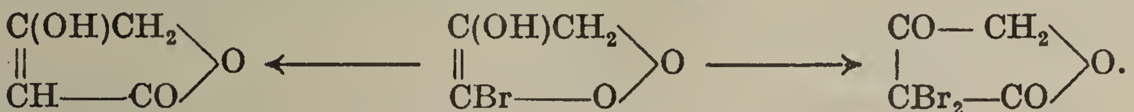


B.

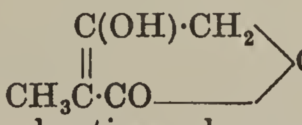


Conrad and *Gast* favour the hydroxyl formula, through indirect evidence, namely: that they prepared the lactone of γ-hydroxydialkylacetoacetic acids from dialkylacetoacetic esters through the γ-bromo ester, and they showed that these true keto-lactones differ throughout in boiling-point and chemical behaviour from tetronic acid and the α-alkyl tetronic acids.

Tetronic acid, (1) (below) is prepared from synthetic tetronic carboxylic ester, by hydrolysis, and elimination of CO_2 (Ber. **36**, 471); also by reduction by sodium amalgam of α-*bromotetronic acid*, (2) the decomposition product of αγ-dibromoacetoacetic ester. *Dibromotetronic acid*, (3) is obtained from bromotetronic acid and bromine. It slowly decomposes into bromotetronic acid and tribromomethyl-ketol (above), with elimination of CO_2.

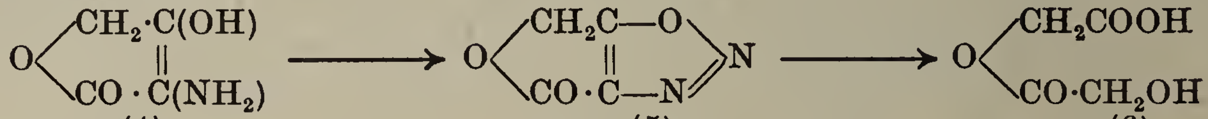


(1) (2) (3)

Tetrinic acid, α-*methyltetronic acid*,  , m.p. 189°, b.p. 292°, with partial decomposition, results on heating γ-bromomethylacetoacetic ester or by treating it with alcoholic potassium hydroxide. Heated with water to 200°, it breaks down into ethyl ketol (p. 394) and CO_2, and when it is boiled with barium hydroxide it yields glycollic acid and propionic acid. Chromic acid oxidizes it to diacetyl and CO_2 (Ann. **288**, 1).

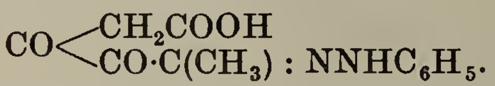
Pentinic acid, α-ethyltetronic acid, m.p. 128°. *Hexinic acid, α-propyltetronic acid,* m.p. 126°. *Heptinic acid, α-isobutyltetronic acid,* m.p. 150°.

The tertiary methinic group of the tetronic acid (formula 1, above) and the methylene group in the diketone formula (A. above) react most actively with other substances: iodine produces directly *iodotetronic acid*; fuming sulphuric gives rise to *sulphotetronic acid.* Nitrous acid gives *oximinotetronic acid, oximinoketobutyrolactone,* $(C_4H_2O_3):NOH$, m.p. 136° (decomp.), which on oxidation yields *nitrotetronic acid,* $(C_4H_2O_3):NOOH$, m.p. 195° (decomp.); this substance can also be prepared directly from tetronic acid and nitric acid. Reduction of the nitro compound produces *aminotetronic acid* (4), from which nitrous acid produces *diazotetronic anhydride* (5), m.p. 93°. It is stable towards acids, but with alkalis generates nitrogen and forms *glycolloglycollic acid* (6), m.p. 100° (p. 420):



(4) (5) (6)

Tetronic acid reacts with diazobenzene salts to form *diketobutyrolactone phenylhydrazone,* $(C_4H_2O_3):NNHC_6H_5$, which is isomerized by alkalis to salts of benzene azotetronic acid. α-Methyltetronic acid is converted by diazobenzene salts into *glycolylpyroracemic acid phenylhydrazone,* with rupture of the ring:



$$CO\begin{cases}CH_2COOH\\CO{\cdot}C(CH_3):NNHC_6H_5.\end{cases}$$

Aldehydes and ketones unite very readily with two molecules of tetronic acid to form *alkylidene bis-tetronic acids,* $(C_4H_3O_3)_2CRR_1$, substances from which further condensation produces a series of interesting cyclic compounds (see Vol. II) (Ann. **312**, 119: **322**, 351).

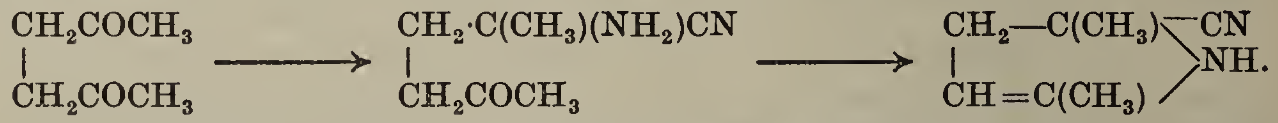
Ethoxyacetoacetic ester, $(C_2H_5O)CH_2COCH_2COOC_2H_5$ or $CH_3{\cdot}CO{\cdot}CH(OC_2H_5){\cdot}CO_2C_2H_5$, b.p. 105°/44 mm., is formed by reduction of ethoxychloroacetoacetic ester, the condensation product of chloroacetic ester and sodium (Ann. **269**, 15).

γ-Methoxydimethylacetoacetic ester, $(CH_3O)CH_2{\cdot}CO{\cdot}C(CH_3)_2CO_2C_2H_5$, m.p. 70°, b.p. 241°, is prepared from γ-bromodimethylacetoacetic ester and sodium methoxide in methyl alcohol (Ber. **30**, 856).

γ-Acetoxy-α-acetylbutyric ester, $C_2H_3O{\cdot}OCH_2{\cdot}CH_2CH(COCH_3)CO_2CH_3$, b.p. 150–153°/12 mm., is formed from glycol bromoacetin (p. 373) and sodium acetoacetic ester (C. 1904, II. 586).

α-Hydroxylævulinic acid, $CH_3CO{\cdot}CH_2CH(OH)CO_2H$, m.p. 103°, and *β-hydroxylævulinic acid,* $CH_3COCH(OH)CH_2CO_2H$, an oil, are prepared from the corresponding bromolævulinic acids (Ann. **264**, 259). Chloral acetone (p. 394) may be considered as being the orthotrichloride of the first of these acids.

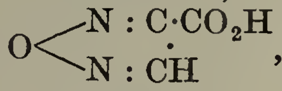
α-Amino-α-methyllævulinic acid; the *nitrile* (formula, see below), b.p. 108°/17 mm., is formed from acetonylacetone (p. 405) and ammonium cyanide. It readily loses water and passes into a cyclic imine or pyrroline derivative (Ber. **40**, 2886):

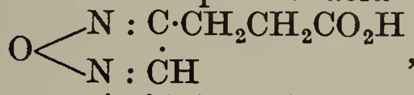
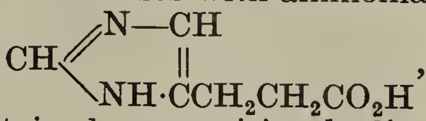


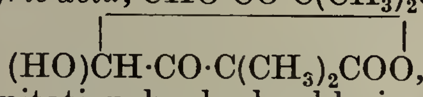
Ketohydroxystearic acid, $CH_3[CH_2]_5CH(OH)CH_2CH_2CO[CH_2]_7COOH$, m.p. 84°, is obtained from ricinostearolic acid (p. 354). An *isomeric* ketohydroxystearic acid, m.p. 64°, is obtained by oxidizing oleic acid with permanganate in neutral solution (Ber. **36**, 2657).

13. ALDEHYDOKETONE CARBOXYLIC ACIDS

Glyoxalcarboxylic acid, mesoxalic semialdehyde, $CHO{\cdot}CO{\cdot}CO_2H$, is formed by the oxidation of tartaric acid by chlorine in the presence of ferrous salts; also from dihydroxymaleic acid (*q.v.*) and ferric sulphate (C. 1902, I. 857, 978). Uric acid may be looked upon as the diureide of this half-aldehyde of mesoxalic acid.

Di-isonitrosopropionic acid, $HON:CH\cdot C(:NOH)\cdot CO_2H$, is the dioxime of glyoxylcarboxylic acid. It is obtained from dibromopyroracemic acid. It is known in two modifications, m.p. 143° and 172° (Ber. **25**, 909). *Furazancarboxylic acid*,  $O\!<\!\begin{matrix}N:C\cdot CO_2H\\ N:\dot{C}H\end{matrix}$, m.p. 107°, is the anhydride of this dioxime. It results from the oxidation of furazanpropionic acid with $KMnO_4$. Sodium hydroxide causes it to rearrange itself into *iso*nitrosocyanoacetic acid (Ann. **260**, 79: Ber. **24**, 1167). *Osazone* of glyoxylcarboxylic acid, $CH(NNHC_6H_5)C(NNHC_6H_5)COOH$, m.p. 223°.

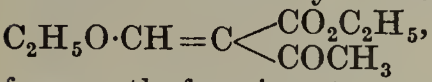
Glyoxylpropionic acid, $HCO\cdot CO\cdot CH_2CH_2CO_2H$, results, together with diacetyl, when $\beta\delta$-dibromolævulinic acid is boiled with water. It forms a yellow varnish. It passes into succinic acid upon oxidation. *Oxime*, $HC(:NOH)\cdot C(:NOH)\cdot CH_2\cdot CH_2\cdot CO_2H$, m.p. 136°. Concentrated sulphuric acid changes it into the anhydride, *furazanpropionic acid*,  $O\!<\!\begin{matrix}N:C\cdot CH_2CH_2CO_2H\\ N:\dot{C}H\end{matrix}$, m.p. 86°. Sodium hydroxide converts this acid into cyanoximidobutyric acid (p. 623), whilst with potassium permanganate it yields furazancarboxylic acid. In the form of a keto-aldehyde (see pp. 399, 401), glyoxylpropionic acid condenses with ammonia and formaldehyde to a *glyoxaline propionic acid*,  $CH\!\begin{matrix}\nearrow N—CH\\ \qquad\quad \|\\ \searrow NH\cdot CCH_2CH_2CO_2H\end{matrix}$, which is also produced from *histidine*, one of the protein decomposition bodies (C. 1905, II. 830: 1908, II. 606).

Glyoxylisobutyric acid, $CHO\cdot CO\cdot C(CH_3)_2COOH$, m.p. 138°, is obtained from the isomeric *lactone*,  $(HO)\overline{CH\cdot CO\cdot C(CH_3)_2COO}$, m.p. 168°, by solution in soda and subsequent precipitation by hydrochloric acid.

The lactone was obtained on treating γ-methoxydimethylacetoacetic ester with bromine, and then decomposing the monobromosubstitution product with water (Ber. **30**, 856).

Derivatives of an aldehydo-keto-carboxylic acid, $CHO\cdot CH_2CO\cdot CO_2H$ (or an unsaturated hydroxy-aldehydic acid, $CHO\cdot CH:C(OH)CO_2H$), are probably exemplified by muco-hydroxy-chloric acid and muco-hydroxy-bromic acid (p. 457) (Am. Chem. J. **9**, 148, 160).

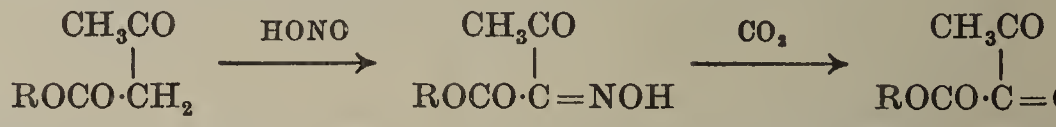
Formylacetoacetic acid, $CHO\cdot CH(COCH_3)COOH$, and in its desmotropic *enol*-forms, $HOCH:C(COCH_3)COOH$, and $CH_3C(OH):C(CHO)CO_2H$, is the hypothetical acid from which may, perhaps, be derived

Hydroxymethyleneacetoacetic ester,  $HOCH{=}C\!<\!\begin{matrix}CO_2C_2H_5\\ COCH_3\end{matrix}$, b.p. 95°/21 mm., which is formed by the action of water on ethoxymethyleneacetoacetic ester,  $C_2H_5O\cdot CH{=}C\!<\!\begin{matrix}CO_2C_2H_5\\ COCH_3\end{matrix}$, b.p. 150°/15 mm. The latter substance is obtained from orthoformic ester and acetoacetic ester by heating them with acetic anhydride (Ber. **26**, 2730). Hydroxymethyleneacetoacetic ester is a strong acid (see hydroxymethylene acetyl acetone, p. 592); it is readily soluble in alkali acetates, but is insoluble in water; *copper salt*, m.p. 156°. Ethoxymethyleneacetoacetic ester is converted by ammonia into *aminomethyleneacetoacetic ester* $(C_6H_8O_3){=}CH\cdot NH_2$, m.p. 55°, and combines with acetoacetic ester to form methenyl bis-acetoacetic ester, $(C_6H_8O_3):CH(C_6H_9O_3)$, m.p. 96°. The latter is converted by ammonia into lutidine dicarboxylic ester (Vol. II); and by sodium ethoxide into *m*-hydroxyuvitic acid (*L. Claisen*, Ann. **297**, 14). When alkoxymethyleneacetoacetic esters are melted with sodium acetoacetic ester, two dyes of undetermined structure are formed—*xanthophanic acid* and *glaucophanic acid* (Ber. **39**, 2071).

14. DIKETOCARBOXYLIC ACIDS

Paraffin Diketocarboxylic Acids.—*αβ-Diketobutyric acid, acetylglyoxylic acid*, $CH_3CO\cdot CO\cdot COOH$. The acid is unknown in the free state, but the esters are obtained when acetoacetic esters are acted on by N_2O_3, in acetic anhydride and ether solution. The esters are orange-yellow, mobile liquids (*cf.* α-Diketones and α-Triketones, p. 592), which combine with water to form colourless crystalline hydrates: *methyl ester*, b.p. 65–68°/12 mm., $+ H_2O$, m.p. 80°; *ethyl ester*, b.p. 70°/13 mm., + ½H_2O, m.p. 148°; iso*butyl ester*, b.p. 96–100°/18 mm., + ½H_2O, m.p. 115–120°.

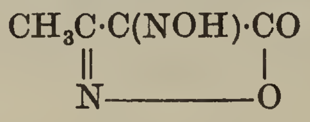
iso*Nitroso-acetoacetic ester*, $CH_3COC(NOH)CO_2R$, is an intermediate product in the formation of the above esters. The *ethyl ester*, m.p. 56°, b.p. 155°/15 mm., can be isolated by treating acetoacetic ester in acetic acid solution with ice-cold sodium nitrite solution; the action of NO_2 converts it into the diketobutyric ester (C. 1905, I. 1591: II. 34):



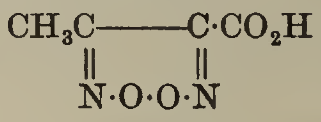
$$\begin{matrix} CH_3CO \\ | \\ ROCO{\cdot}CH_2 \end{matrix} \xrightarrow{\text{HONO}} \begin{matrix} CH_3CO \\ | \\ ROCO{\cdot}C{=}NOH \end{matrix} \xrightarrow{CO_2} \begin{matrix} CH_3CO \\ | \\ ROCO{\cdot}C{=}O \end{matrix}$$

*iso*Nitroso-acetoacetic ester is also formed from acetylmalonic ester (p. 619) and nitrous acid. One molecule of hydroxylamine produces *αβ-di-*iso*nitroso-butyric ester*, $CH_3C(NOH){\cdot}C(NOH)CO_2C_2H_5$, m.p. 161°, which is changed by hydrochloric acid into iso*nitroso-methyl-isoxazolone* (1), m.p. 159°, whilst nitric acid causes the formation of a *peroxide* (2), m.p. 92° (Ber. **28**, 2683: **38**, 926); which probably has the furoxan constitution (3):

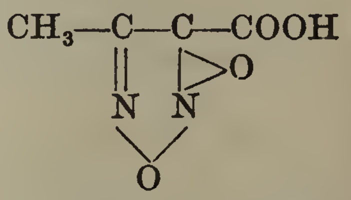
(1)



(2)



(3)



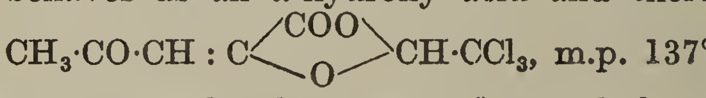
β-Phenylhydrazone, $CH_3C(NNHC_6H_5){\cdot}CO{\cdot}CO_2C_2H_5$, m.p. 103°, is formed from diketobutyric ester and one molecule of phenylhydrazine in the cold. *α-Phenylhydrazone*, $CH_3CO{\cdot}C(NNHC_6H_5)CO_2C_2H_5$, m.p. 154°, is prepared from sodium acetoacetic ester and diazo-benzene salts; with phenylhydrazine it forms the *osazone*, m.p. 209° (Ann. **247**, 205: C. 1904, II. 588).

βγ-Diketovaleric acid, $CH_3CO{\cdot}CO{\cdot}CH_2CO_2H$, is unknown; but its derivative, *β-*iso*nitrosolævulinic acid*, $CH_3CO{\cdot}C(NOH)CH_2CO_2H$, m.p. 119° (decomp.), is formed from acetosuccinic ester (p. 622). When fused, it loses CO_2 and changes into *iso*nitroso-ethyl-methyl-ketone (p. 407).

α-Diketocarboxylic acids include also *stearoxylic acid*, and *behenoxylic acids*, etc., which have already been referred to (p. 352).

θλ-Diketostearic acid, m.p. 96°, is obtained from ricinostearolic acid (p. 354) (C. 1907, I. 916).

β-Diketocarboxylic Acids.—*Acetylpyroracemic ester*, *acetoneoxalic ester*, *αγ-diketovaleric ester*, $CH_3CO{\cdot}CH_2CO{\cdot}CO_2C_2H_5$, is formed from one molecule of acetone, one molecule of oxalic ester, and sodium ethoxide solution (C. 1908, I. 1379). Ferric chloride produces a dark-red colour. The free acid liberated from the ester condenses to *sym.*-hydroxytoluic acid, $CO_2HC_6H_3(OH)CH_3$ (Ber. **22**, 3271). Acetoneoxalic ester and phenylhydrazine form *phenylpyrazolecarboxylic ester*, m.p. 133° (Ann. **278**, 278). With chloral it behaves as an α-hydroxy acid and there results *acetylpyroracemic chloralide*,



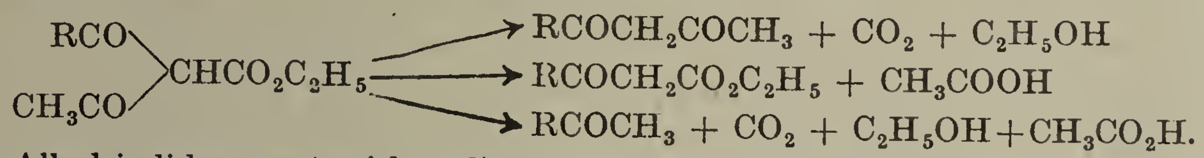
$CH_3{\cdot}CO{\cdot}CH : C\!\begin{matrix} \diagup COO \diagdown \\ \diagdown\, O\, \diagup \end{matrix}\!CH{\cdot}CCl_3$, m.p. 137° (Ber. **31**, 1305).

Besides acetone, other ketones, such as ethyl methyl ketone, *iso*butyl and butylmethyl ketones, react with oxalic ester and sodium alcoholate to form *propionylpyroracemic ester*, $CH_3CH_2CO{\cdot}CH_2COCO_2C_2H_5$ (?), b.p. 73–78°/0·6 mm.; *acid*, m.p. 83° (Ber. **39**, 1333), iso*butyrylpyroracemic ester*, $(CH_3)_2CHCO{\cdot}CH_2{\cdot}COCO_2C_2H_5$, and *butyrylpyroracemic ester*, $CH_3CH_2CH_2COCH_2COCO_2C_2H_5$ (C. 1902, II. 189: 1903, I. 138) respectively.

Diacylacetic Esters.—The hydrogen in acetoacetic ester can not only be replaced by alkyls, as abundantly shown above, but also by acid radicals (*cf.* p. 474), by acting with acid chlorides on the sodium compound suspended in ether.

α-Acetylacetoacetic ester, *diacetylacetic ester*, $(CH_3CO)_2CHCO_2C_2H_5$, b.p. 123°/50 mm., is prepared by the action of acetyl chloride as indicated above; by the transformation of the isomeric β-acetoxycrotonic ester by means of K_2CO_3, or by heat (p. 474); by the action of alcohol on the reaction product of $AlCl_3$ and acetyl chloride, $(CH_3CO)_2CH{\cdot}CCl_2OAlCl_2$ (p. 403) (*Gustavson*, Ber. **21**, R. 252). The *anilide*, $(CH_3CO)_2CH{\cdot}CONHC_6H_5$, m.p. 119°, results from the union of diacetyl methane with phenyl *iso*cyanate, and a trace of alkali (Ber. **37**, 4627: **38**, 22). The diacetoacetic ester, like acetoacetic ester itself, forms metallic derivatives. Water at ordinary temperatures slowly converts it into acetic acid and acetoacetic ester: sodium ethoxide causes the displacement of the acetyl group with the formation of acetic ester and sodium acetoaetic ester. Pyridine and acetyl chloride form an O-*acetate*, $CH_3C(OCOCH_3):C(COCH_3)CO_2C_2H_5$, b.p. 143°/10 mm. (Ber. **33**, 1245). *Cyanoacetylacetone*, see Acetyl acetone (p. 403). *Methyldiaceto-acetic ester* and *ethyldiacetoacetic ester* are volatile only under reduced pressure.

Diacylacetoacetic esters containing two different acid radicals can be decomposed in three ways (*cf.* pp. 258, 403, 471). When such an ester is treated with water at 148–150°, there are formed diacylmethanes, CO_2, and alcohol; ammonia or fixed alkali in the cold produces mono-acyl-acetic ester and acetic acid; heated with hydrochloric at 130–140° it breaks down into alkyl methyl ketone, CO_2, acetic acid, and alcohol (C. 1903, I. 225):



$$\begin{matrix} RCO \\ CH_3CO \end{matrix}\!\!>CHCO_2C_2H_5 \begin{cases} \rightarrow RCOCH_2COCH_3 + CO_2 + C_2H_5OH \\ \rightarrow RCOCH_2CO_2C_2H_5 + CH_3COOH \\ \rightarrow RCOCH_3 + CO_2 + C_2H_5OH + CH_3CO_2H. \end{cases}$$

Alkyl iodides react with sodium diacylacetic esters and form acylalkylacetic esters by replacement of the acetyl group (C. 1904, II. 25).

Propionylacetoacetic ester, $C_2H_5COCH(COCH_3)CO_2C_2H_5$, b.p. 111°/20 mm.; *copper salt*, m.p. 89°. n-*Butyrylacetoacetic methyl ester*, b.p. 105°/14 mm. iso-*Butyrylacetoacetic ester*, b.p. 114°/15 mm. *Caproylacetoacetic ester*, b.p. 136°/10 mm. *Butyryl* iso*butyrylacetic ester*, $CH_3CH_2CH_2COCH[COCH(CH_3)_2]CO_2C_2H_5$, b.p. 125°/18 mm.

ββ-Diacetopropionic ester, $(CH_3CO)_2CHCH_2CO_2C_2H_5$, b.p. 147°/24 mm., *ββ-diaceto*iso*butyric ester*, $(CH_3CO)_2CHCH(CH_3)CO_2C_2H_5$, b.p. 150°/33 mm., *γγ-diacetobutyric methyl ester*, $(CH_3CO)_2CHCH_2CH_2CO_2CH_3$, b.p. 161°/24 mm., are formed from sodium acetyl acetone and chloroacetic ester, α-bromopropionic ester, and β-bromopropionic ester, respectively. Sodium alcoholate decomposes diacetopropionic ester into acetic ester and lævulinic ester; sodium alcoholate and iodomethane break it down into acetic ester and β-methyl lævulinic ester. Diacetobutyric ester undergoes similar changes (C. 1902, II. 345).

γ-Acetylacetoacetic acid, *triacetic acid*, is prepared in the form of its *lactone*, $CH_3C:CHCO{\cdot}CH_2COO$, by heating dehydracetic acid (*q.v.*) with sulphuric acid (Ber. **34**, R. 857). When heated with acetic anhydride and sodium acetate it is then reconverted into dehydracetic acid (Ber. **37**, 338: C. 1905, I. 348: 1906, II. 1044).

γ-Acetyldimethylacetoacetic methyl ester, α-dimethyltriacetic ester, $CH_3CO{\cdot}CH_2{\cdot}COC(CH_3)_2CO_2CH_3$, is formed, together with *iso*butyric ester, from dimethylacetoacetic methyl ester and sodium at 115–125° (Ber. **31**, 1339).

γ-Acetyl-α-dimethylacetoacetic ester is similarly formed from diethyl acetoacetic ester and sodium ethoxide (Ber. **33**, 2683).

γ-Diketocarboxylic Acids.—*Acetonylacetoacetic ester*, *αβ-diacetopropionic ester*, $CH_3COCH_2{\cdot}CH(COCH_3)CO_2C_2H_5$, is formed from chloroacetone and sodium acetoacetic ester. Fuming hydrochloric acid turns it into pyrotritaric ester (Ber. **17**, 2759). When heated with water to 160° the ester yields acetonyl acetone (p. 405).

Acetonyllœvulinic acid, $CH_3COCH_2CH_2COCH_2{\cdot}CH_2CO_2H$, m.p. 75°, is formed from furfuracetone (Vol. II) when heated with hydrochloric acid (Ber. **32**, 1176).

Unsaturated diketocarboxylic acids, *β-mesityl oxide oxalic acid*, $(CH_3)_2C:CH{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CO_2H$, m.p. 166° (decomp.). Potassium hydroxide liberates it from either its *ethyl ester*, m.p. 59°, b.p. 143°/11 mm., or its *methyl ester*, m.p. 67°. On allowing sodium in ether to act on molecular quantities of mesityl oxide and oxalic ester, then acidifying with dilute sulphuric acid and distilling, a mixture of α- and β-mesityl oxide oxalic esters results. It can be separated by means of a sodium carbonate solution, in which the α-ester alone is soluble. Ferric chloride turns this a blood-red.

α- or aci-*Mesityl oxide oxalic ethyl ester*, $Me_2C:CH{\cdot}CO{\cdot}CH:C(OH){\cdot}CO_2Et$, m.p. 21°, gives a blood-red coloration with ferric chloride. Potassium hydroxide solution liberates the corresponding *acid*, m.p. 92° (Ann. **291**, 111, 137). The α-acid in alcoholic solution (more slowly in ether) passes into the β-modification.

15. MONOHYDROXY-DICARBOXYLIC ACIDS

A. MONOHYDROXY-PARAFFIN DICARBOXYLIC ACIDS

$C_nH_{2n-1}(OH)(CO_2H)_2$

Numerous saturated monocarboxylic acids are known: thus, the hydroxymalonic acid group corresponds with the malonic acid group, hydroxysuccinic acid group with the succinic acid group, hydroxyglutaric acid group with the glutaric acid group, etc.

There are many representatives of these acids in which the hydroxyl group occupied the γ-position with reference to the carboxyl group, and these acids like the γ-hydroxymonocarboxylic acids, when separated from their salts, readily part with water and become lactones. In general, the alcoholic hydroxyl group is introduced into the dibasic acids, just as it is done in the case of the monobasic acids. The formation of the alkylparaconic acids, which are γ-lactone acids (p. 612), by the condensation of aldehydes with succinic acid and alkylsuccinic acids (p. 547), is worthy of note.

Hydroxymalonic Acid Group

Tartronic acid, *hydroxymalonic acid* [propanol diacid], $CH(OH)(COOH)_2$, is produced: (1) From glycerol by oxidation with potassium permanganate; (2) from chloro- and bromo-malonic acid by the action of silver oxide or by hydrolysis of their esters with alkalis; (3) from trichlorolactic acid when the latter is digested with alkalis (Ber. **18,** 754, 2852); (4) from dibromopyroracemic acid when digested with barium hydroxide solution; (5) from mesoxalic acid (p. 617) by the action of sodium amalgam. (6) *Nucleus synthesis:* from glyoxylic acid (p. 455) by the action of HNC and hydrochloric acid, (7) by the spontaneous decomposition of nitrotartaric acid and of dihydroxytartaric acid. It can be conveniently prepared from tartaric acid by allowing it to remain in contact with nitric acid and P_2O_5 (Ann. **416,** 233).

Its formation from nitrotartaric acid, described in 1854 by Dessaignes, has given it the name tartronic acid.

Tartronic acid is easily soluble in water, alcohol, and ether, and crystallizes in large prisms, m.p. 156–158° (Ann. **416,** 233). On melting it is decomposed into carbon dioxide and polyglycollide, $(C_2H_2O_2)x$ (p. 420) (Ber. **18,** 756).

The *calcium salt,* $C_3H_2O_5Ca$, and *barium salt,* $C_3H_2O_5Ba + 2H_2O$, dissolve with difficulty in water, and are obtained as crystalline precipitates.

Ethyl ester, $CH(OH)(CO_2C_2H_5)_2$, b.p. 222–225° (Ber. **18,** 2853); *acetyl* derivative, b.p. 158–163°/62 mm. (Ber. **24,** 2997).

Ethoxymalonic acid, $C_2H_5O{\cdot}CH(CO_2H)_2$, m.p. 124°; *ethyl ester* is formed from ethoxyacetic ester (*q.v.*).

Chloral- and bromal-cyanohydrins (p. 433) and trichlorolactic acid (p. 421) may be looked on as being derivatives of tartronic acid. See also Chloro- and Bromo-malonic ester (p. 544).

Alkyltartronic acids.—*Methyltartronic acid,* iso*malic acid, α-hydroxy*iso*succinic acid,* $CH_3C(OH)(CO_2H)_2$, is obtained (1) by the action of silver oxide on bromo*iso*succinic acid; (2) when hydrocyanic acid acts on pyroracemic acid; pyroracemic ester and hydrocyanic acid produce the *nitrile ester,* $CH_3C(OH)(CN)CO_2C_2H_5$, m.p. 105°/19 mm., which is converted on hydrolysis to *iso*malic acid (C. 1899, I. 1206: Ber. **39,** 1858); (3) diacetyl cyanide (p. 464), the acetate of methyltartrodinitrile, $CH_3C(OCOCH_3)(CN)_2$, is hydrolysed by fuming hydrochloric acid to methyltartronic acid (Ber. **26**, R. 7 : **27**, R. 510). The acid breaks down into CO_2 and lactic acid when it is heated to 140°.

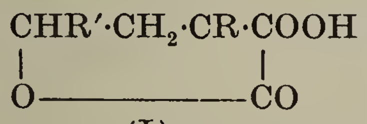
Ethyltartronic acid, $C_2H_5C(OH)(CO_2H)_2$, m.p. 98°, is formed (1) on boiling ethyl chloromalonic ester with barium hydroxide solution (p. 544) ; (2) from dipropionyl cyanide (p. 465) ; (3) by the action of ethyl iodide on sodium acetotartronic ester (Ber. **24**, 2999). When heated above its melting point it breaks down into CO_2 and α-hydroxybutyric acid.

Propyltartronic acid, $CH_3CH_2CH_2\cdot C(OH)(CO_2H)_2 + H_2O$, m.p. 52–56°, and iso*propyltartronic acid*, decomposes at 149°, are formed by the hydrolysis of dibutyryl and di*iso*butyryl dicyanide (p. 465) (Ber. **28**, R. 295).

α-*Amino*iso*succinic acid*, $CH_3\cdot C(NH_2)(COOH)_2$, results when pyroracemic acid is acted on with HCN and alcoholic ammonia (Ber. **20**, R. 507).

β-*Hydroxy*iso*succinic acid*, $CH_2OH\cdot CH(CO_2H)_2$, a syrup, is produced by hydrolysis of the reaction product of chloromethyl ether (p. 243) and sodium malonic ester. It decomposes at 113° into H_2O, CO_2, and acrylic acid (C. 1904, II. 641) ; *ethyl ester*, $C_2H_5OCH_2\cdot CH(CO_2H)_2$, has been obtained from methylene malonic ester (p. 564) by the action of alcoholic potassium hydroxide (Ber. **23**, R. 194).

γ-Hydroxyalkylmalonic Acids.—The following γ-hydroxyalkylmalonic acids are only known in the form of alkali or alkali earth salts. These are produced when the corresponding γ-lactone carboxylic acids are treated with alkali hydroxides or the hydroxides of the alkali earths. The γ-lactonic acids can easily be obtained from these salts ; these salts are produced by treatment with carbonates :



$$\begin{array}{l}CHR'\cdot CH_2\cdot CR\cdot COOH\\ |\qquad\qquad\qquad\; |\\ O\text{—————}CO\end{array}$$

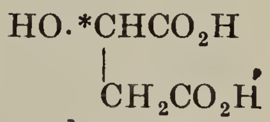
(I)

Butyrolactone-α-carboxylic acid, (I, above, RR′ = H) is prepared from bromoethylmalonic acid, $BrCH_2CH_2\cdot CH(CO_2H)_2$, m.p. 117° (the hydrobromide addition product of vinaconic acid, trimethylene-1 : 1-dicarboxylic acid), when it is heated with water ; also on digesting the latter with dilute sulphuric acid (Ann. **227**, 31). Heated to 120°, butyrolactonecarboxylic acid breaks down into CO_2 and butyrolactone (p. 427). The *ethyl ester*, b.p. 175°/25 mm., is formed by the combination of ethylene oxide and sodium malonic ester, whereby *hydroxyethylmalonic ester* is produced, which immediately loses alcohol to form a lactone. Ammonia converts the lactone ester into *β-hydroxyethylmalonamide*, $HOCH_2CH_2\cdot CH(CONH_2)_2$, m.p. 150° (Ber. **34**, 1976). The *phenyl ether* of *hydroxyethylmalonic acid*, $C_6H_5O\cdot CH_2\cdot CH_2\cdot CH(COOH)_2$, m.p. 142° (Ber. **29**, R. 286).

α-*Methylbutyrolactone-α-carboxylic acid*, (I, above, R = Me, R′ = H), m.p. 98°, results when bromoethyl*iso*succinic ester, the reaction product of ethylene bromide and sodium *iso*succinic ester, is treated with barium hydroxide solution and then acidified (Ann. **294**, 89).

α-*Carbovalerolactonic acid*, *γ-methylbutyrolactone-α-carboxylic acid* (I, above, R = H, R′ = Me) results when allyl malonic acid is acted on with HBr. It breaks down at 200° into CO_2 and γ-valerolactone (p. 427).

Hydroxysuccinic Acid Group



Malic acid, *hydroxysuccinic acid* [butanol diacid], $\begin{array}{l}HO\cdot{}^{*}CHCO_2H\\ |\\ CH_2CO_2H\end{array}$, m.p. 100°. Since malic acid contains an asymmetric carbon atom, it can occur in three modifications : (1) a dextrorotatory form, (2) a lævorotatory form, and (3) an inactive *dl-* variety. This is a compound of equal molecules of the dextro- and lævorotatory modifications.

The *lævo*-variety occurs free or in the form of salts in many plant juices, hence it is frequently spoken of as *ordinary malic acid.* It is found free in unripe apples, in grapes, and in gooseberries, also in mountain ash berries (*Sorbus aucuparia*), in *Berberis vulgaris,* and in the sea buckthorn (or sallow thorn), *Hippophaë rhamnoides* (Ber. **32**, 3351). It is obtained from the last-named fruits by means of the calcium salts (Ann. **38**, 257 : Ber. **3**, 966). Calcium hydrogen malate exists in tobacco leaves ; potassium hydrogen malate in the leaves and stalks of rhubarb (C. 1902, I. 1399). On malic acid obtained from the *Crassulaceæ*, see Ber. **31**, 1432.

Historical.—Ordinary malic acid was discovered in 1785 by *Scheele* in unripe gooseberries. *Liebig* ascertained its composition in 1832. *Pasteur*, in 1852, obtained inactive malic acid from inactive aspartic acid, and *Kekulé* (1861) made it from bromosuccinic acid. The *dextro*-acid was first obtained by *Bremer* in the reduction of dextro-tartaric acid.

Formation of optically inactive or dl-*malic acid*, m.p. 130° (Ber. **29**, 1698) :

1. From the mono-ammonium salt of lævo- and dextro-malic acid.
2. By heating fumaric acid to 150–200° with water.
3. When fumaric or maleic acid is heated with sodium hydroxide to 100° (Ber. **18**, 2713).
4. By treating monobromosuccinic acid with silver oxide and water, with water alone, with dilute hydrochloric acid, or with dilute sodium hydroxide at 100° (Ber. **24**, R. 970).
5. By the action of N_2O_3 on inactive aspartic acid.
6. By the reduction of racemic acid with hydriodic acid.
7. When oxaloacetic ester is reduced with sodium amalgam in acid solution (Ber. **24**, 3417 : **25**, 2448).
8. By the action of potassium hydroxide on the reaction-product of KNC and β-dichloropropionic ester.
9. By saponifying the esters of chloroethanetricarboxylic acid.
10. When potassium hydroxide acts on γ-trichloro-β-hydroxybutyric acid, $CCl_3CH(OH)CH_2CO_2H$, the reaction-product of chloral and malonic acid under the influence of glacial acetic acid or pyridine (Ber. **25**, 794 : **38**, 2733).

The identity of the acids from 1 to 6 has been proved by means of the well-crystallized mono-ammonium salt, $C_4H_5O_5NH_4 + H_2O$, of the inactive acid (Ber. **18**, 1949, 2170).

Formation of the lævo- *and* dextro- *forms :* Both acids can be produced by resolution of the inactive malic acid by cinchonine (Ber. **13**, 351 : **18**, R. 537). The *dextro*-acid has also been obtained by reduction of the natural (+)-*d*-tartaric acid with hydriodic acid, or by milder reactions by converting the tartaric acid into chloromalic acid and reducing the latter (Ber. **55**, 1339) or from *dextrorotatory*-aspartic acid and nitrous acid. These relationships with *d*-tartaric acid justify the description of the dextrorotatory malic acid as *d*-malic acid, and the naturally occurring (—) form as *l*-malic acid. This acid is similarly formed from *l*-asparagine and *l*-aspartic acid (Ber. **28**, 2772). The two malic acids can be interconverted into their optical isomers by converting them by means of phosphorus pentachloride into the chlorosuccinic acids and treating the latter with moist silver oxide. (Walden inversion ; Walden, Ber. **29**, 133.) For a discussion of the rearrangement at the asymmetric carbon atom, see Ber. **61**, 509.

Properties.—Malic acid forms deliquescent crystals, m.p. 100°, which dissolve readily in alcohol, slightly in ether.

Reactions.—(1) When heated to 100° anhydro-acids are formed (Ber. **32**, 2706) ; at 140–150° mainly fumaric acid results ; when rapidly heated to 180° it decomposes into water, fumaric acid, and maleic anhydride (pp. 565, 566). Prolonged boiling with aqueous sodium hydroxide converts malic acid partially into fumaric acid (Ber. **33**, 1452). (2) Oxidation with permanganate or hydrogen peroxide in presence of ferrous salts produces oxaloacetic acid (p. 619), while chromic acid produces malonic acid. (3) Reduction gives rise to succinic acid. It results from the fermentation of the calcium salt by yeast, of the free acid by *Bacillus aerogenes* (Ber. **32**, 1915), and when the acid is heated to 130° with hydriodic acid (p. 547). (4) Heating with hydrobromic acid produces bromosuccinic acid ; *l*-malic acid and PCl_5 at ordinary temperatures yield (+)-chlorosuccinic acid (Ber. **61**, 504) which, with moist silver oxide, changes into *d*-malic acid (pp. 555, 606). (5) When heated alone or with sulphuric acid or zinc chloride, it is converted into coumalic acid (p. 616). (6) On being heated with phenol and sulphuric acid, coumarin results ; it is possible that the semi-aldehyde of malonic acid, $CHO{\cdot}CH_2{\cdot}CO_2H$, is first formed, with which the phenol then condenses (Ber. **27**, 1646).

Salt and esters of dl-*malic acid : Mono-ammonium malate*, $C_4H_5O_5NH_4 + H_2O$ (Ber. **18**, 1949 2170). Resolution into the optical components (Ber. **31**, 528). dl-*Malic diethyl ester*, $C_2H_3(OH)(CO_2C_2H_5)_2$, b.p. 255° (Ber. **25**, 2448).

Salts of the lævo-*acid, malates : Mono-ammonium salt*, $C_4H_5O_5(NH_4)$, when exposed to a temperature of 160–200°, becomes converted into so-called fumarimide (Ann. **239**, 159 note). *Neutral calcium malate*, $C_4H_4O_5Ca + H_2O$, separates as a crystalline powder on boiling. The *acid salt*, $(C_4H_5O_5)_2Ca + 6H_2O$, forms large crystals which are not very soluble in cold water, but are more soluble in hot (Ber. **19**, R. 679).

l-*Malic ethers and esters :* The dialkyl esters are prepared from malic acid, alcohols, and hydrochloric acid. They can be distilled unchanged (Z. physik. Chem. **16**, 494), but when slowly heated pass into fumaric esters (Ber. **18**, 1952). Reaction with PCl_5 and PBr_5 in chloroform changes them into (+)-chloro- and (+)-bromosuccinic esters (p. 555). Attempts to prepare malic esters by means of the silver salt of the acid result in the partial substitution of the hydroxyl hydrogen by the alcoholic radical (C. 1899, I. 779).

The optical rotatory power of many of these esters has been determined ; they are lævorotatory (Ber. **28**, R. 725 : **29**, R. 164, C. 1897, I. 88) :

l-Malic methyl ester,	b.p. 122°/12 mm. ;	$[\alpha]_D = -\ 6{\cdot}88$,	$[M]_D = -11{\cdot}15$
l-Malic ethyl ester,	,, 129°/12 ,, ;	$[\alpha]_D = -10{\cdot}64$,	$[M]_D = -20{\cdot}22$
l-Malic *n*-propyl ester,	,, 150°/12 ,, ;	$[\alpha]_D = -11{\cdot}60$,	$[M]_D = -25{\cdot}29$
l-Malic *n*-butyl ester,	,, 170°/12 ,, ;	$[\alpha]_D = -10{\cdot}72$,	$[M]_D = -26{\cdot}38$

Triethyl ether-ester, $C_2H_5O{\cdot}C_2H_3(CO_2C_2H_5)_2$, b.p. 119°/15 mm. (Ber. **13**, 1394).

Acetylmalic acid, $CH_3CO{\cdot}OC_2H_3(CO_2H)_2$, m.p. 132° ; *dimethyl ester*, $CH_3CO{\cdot}OC_2H_3(CO_2CH_3)_2$, when slowly distilled at the ordinary pressure, yields fumaric dimethyl ester. *Acetylmalic anhydride*, $CH_3CO{\cdot}OC_2H_3(C_2O_3)$, m.p. 54°, b.p. 161°/14 mm., decomposes when distilled at the ordinary pressure into maleic anhydride and acetic acid (Ann. **254**, 166).

Acetyl-*l*-malic methyl ester,	b.p. 132°/12 mm. ;	$[\alpha]_D = -22{\cdot}86$,	$[M]_D = -46{\cdot}64$
Acetyl-*l*-malic ethyl ester,	,, 141°/12 ,, ;	$[\alpha]_D = -22{\cdot}60$,	$[M]_D = -52{\cdot}43$
Propionyl-*l*-malic methyl ester,	,, 142°/12 ,, ;	$[\alpha]_D = -23{\cdot}08$,	$[M]_D = -50{\cdot}31$

On the *homologous series of acyl*-l-*malic ethyl esters* and their molecular rotations see Z. physik. Chem. **36**, 129.

"*Nitromalic acid*," $NO_2{\cdot}O{\cdot}CH(COOH){\cdot}CH_2{\cdot}COOH$, needles, m.p. 110–112° (decomp.), is obtained from malic acid and nitrating acid, at a low temperature. (J.A.C.S. **43**, 2084) ; *methyl ester*, m.p. 25° $[\alpha]_D^{20} - 33{\cdot}01°$, and *ethyl ester*, b.p. 148–151° $[\alpha]_D^{13} - 31{\cdot}24°$, are prepared from the *l*-malic esters and nitrosulphuric acid (Ber. **35**, 4363).

Amides of the malic acids. α- and *β-malic mono-amides*, $NH_2CO{\cdot}CH(OH){\cdot}CH_2COOH$ and $HOOC{\cdot}CH(OH)CH_2{\cdot}CONH_2$, and their esters are formed from the malic esters and alcoholic ammonia ; from malamide by partial hydrolysis ; also, from bromosuccinic acid and ammonia, a reaction which may result in this amide, partially or wholly in place of the expected aspartic acid (Ber. **41**, 841). *Mal-*

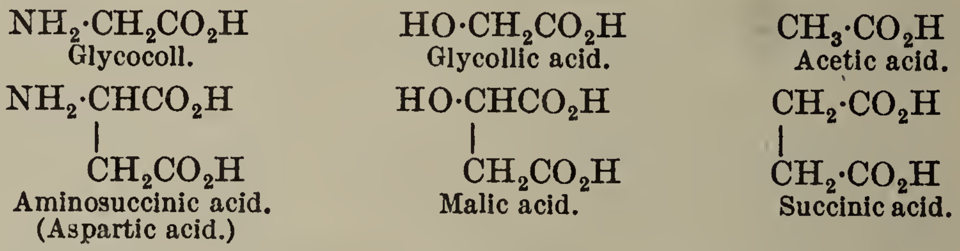
amide, $HO{\cdot}C_2H_3(CONH_2)_2$, is prepared from the monoamidomalic ester and from the malic ester by the action of ammonia (C. 1900, II. 1009). d-*Malamide*, m.p. 156–157° ; *hydrazide*, m.p. 177° ; *azide* from the hydrazide and HNO_2, a yellow oil (J. pr. Chem. [2] 95, 209).

Thiomalic acid, $HOOC{\cdot}CH_2CH(SH)COOH$, m.p. 150°, is formed by the action of ammonia on *xanthosuccinic acid*, $HOOC{\cdot}CH_2CH(SCSOC_2H_5)COOH$, m.p. 149°, which in turn is prepared from bromosuccinic acid and potassium xanthogenate (Ann. **339**, 369 : Ber. **38**, 2687).

Sulphosuccinic acid, $SO_3H{\cdot}C_2H_3(COOH)_2$, is prepared from succinic acid and SO_3 (Ann. **175**, 20) or, better, by addition of bisulphite to maleic or fumaric acid : resolution by strychnine, see Rec. Trav. Chim. **46**, 473.

Aminosuccinic Acids

Aspartic acid bears the same relation to malic and succinic acids as glycocoll bears to glycollic acid and acetic acid ; hence, it may be called aminosuccinic acid :



$NH_2{\cdot}CH_2CO_2H$ Glycocoll. $HO{\cdot}CH_2CO_2H$ Glycollic acid. $CH_3{\cdot}CO_2H$ Acetic acid.

$\begin{array}{l} NH_2{\cdot}CHCO_2H \\ \quad | \\ \quad CH_2CO_2H \end{array}$ Aminosuccinic acid. (Aspartic acid.)

$\begin{array}{l} HO{\cdot}CHCO_2H \\ \quad | \\ \quad CH_2CO_2H \end{array}$ Malic acid.

$\begin{array}{l} CH_2{\cdot}CO_2H \\ | \\ CH_2{\cdot}CO_2H \end{array}$ Succinic acid.

Aminosuccinic acid contains an asymmetric carbon atom, so that like malic acid, it appears in three modifications. The *l*-aminosuccinic acid or *lævo*-aspartic acid is the most important of these. See also *d*- and *l*-chlorosuccinic acid (p. 555) and *d*- and *l*-malic acid (p. 606, etc.).

Inactive *dl*-aspartic acid, *asparacemic acid*, $C_2H_3(NH_2)(CO_2H)_2$, is produced :

(1) By the union of *l*- and *d*-aspartic acids.

(2) On heating active aspartic acid (*a*) with water, (*b*) with alcoholic ammonia to 140–150°, or (*c*) with hydrochloric acid to 170–180° (Ber. **19**, 1694).

(3) When "fumarimide" (p. 607) is boiled with hydrochloric acid.

(4) On heating fumaric and maleic acids with ammonia (Ber. **20**, R. 557 : **21**, R. 644).

(5) By evaporating a solution of hydroxylamine fumarate (Ber. **29**, 1478).

(6) By reducing oximinosuccinic ester with sodium amalgam (Ber. **21**, R. 351).

Benzoylasparacemic acid is resolved into its optical components by means of brucine (Ber. **32**, 2461).

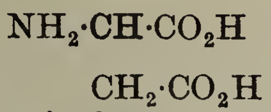
Like glycocoll, aspartic acid combines with alkalis and acids yielding salts. Nitrous acid changes it into inactive malic acid.

dl-*Aspartic diethyl ester*, $NH_2{\cdot}C_2H_3(CO_2C_2H_5)_2$, b.p. 150–154°/25 mm., is produced on heating fumaric and maleic esters with alcoholic ammonia (Ber. **21**, R. 86).

dl-*Aspartic α-mono-ethyl ester*, $COOH{\cdot}CH_2{\cdot}CH(NH_2){\cdot}COOC_2H_5$, m.p. 165° (decomp.), is formed by the reduction of α-oximinosuccinic monoethyl ester and the oxime of oxaloacetic diethyl ester. Ammonia converts it into inactive α-asparagine (constitution, *cf.* p. 610).

dl-*Aspartic β-mono-ethyl ester*, $COOH{\cdot}CH(NH_2){\cdot}CH_2{\cdot}COOC_2H_5$, m.p. 200° (decomp.), is also obtained from the oxime of oxaloacetic ester by reduction with sodium amalgam. A partial saponification occurs at the same time. Ammonia converts it into the two *optically active asparagines*, which are therefore β-aminosuccinamic acids.

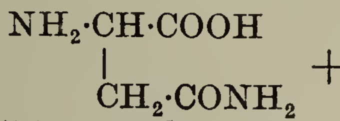
N-*Phenylaspartic acid*, $C_6H_5NH{\cdot}CH(CO_2H)CH_2CO_2H$, m.p. 131°, is formed by the action of bromosuccinic acid on aniline. *Phenylasparaginanil*, C_6H_5-$NHC_2H_3C_2O_2{\cdot}NC_6H_5$, m.p. 210°, results on adding aniline to maleinanil (Ann. **239**, 137).

***l*-Aspartic acid,**  $\begin{array}{c} NH_2\cdot CH\cdot CO_2H \\ CH_2\cdot CO_2H \end{array}$ (configuration, Helv. Chim. Acta. **6**, 411 and 957), occurs in beet molasses, and is procured from proteins in various reactions. It is obtained by the resolution of *dl*-aspartic acid (see above), and from *l*-asparagine by boiling it with alkalis and acids (Ber. **17**, 2929).

It crystallizes in small rhombic leaflets or prisms, and is sparingly soluble in water. Nitrous acid converts it into ordinary *l*-malic acid (Ber. **28**, 2769). *l*-Aspartic acid is lævorotatory in alkaline solutions, and dextrorotatory in acids ; dextro in aqueous solution at low temperatures, and lævo at higher temperatures.

Diethyl ester, b.p. 126°/11 mm., is formed from aspartic acid or asparagines by alcohol and hydrochloric acid (Ber. **34**, 452 : **37**, 4599) ; *dimethyl ester*, b.p. 120°/15 mm. (Ber. **40**, 2058).

***d*-Aspartic acid** results when *d*-asparagine is boiled with dilute hydrochloric acid (Ber. **19**, 1694) and from (—)-chlorosuccinic acid (p. 555).

l- and ***d*-Asparagine,**  $\begin{array}{l} NH_2\cdot CH\cdot COOH \\ | \\ CH_2\cdot CONH_2 \end{array}$ $+ H_2O$ (*l*-(—)-Asparagine : configuration, Ber. **57**, 1547), are the monamides of the two optically active aspartic acids, and are isomeric with malamide (p. 608). Crystallographically, they are identical, including the hemihedral faces (C. 1897, II. 1108).

Historical.—As early as 1805 *Vauquelin* and *Robiquet* discovered the *lævo*-asparagine in asparagus. *Liebig*, in 1833, established its true composition. *Kolbe* (1862) was the first to regard it as the amide of aminosuccinic acid. *Piutti* (1886) discovered *dextro*-asparagine in the sprouts of vetches, in which it occurs together with much *lævo*-asparagine.

l-Asparagine is found in many plants, chiefly in their seeds ; in asparagus (*Asparagus officinalis*), in beet-root, in peas, in beans, and in vetch sprouts, from which it is obtained on a large scale, and also in wheat. *l*- and *d*-Asparagines not only occur together in the sprouts of vetches, but they are found together if asparaginimide, produced from bromosuccinic ester, is heated to 100° with ammonia ; or by the action of alcoholic ammonia on β-aspartic ester (Ber. **20**, R. 510 : Ber. **22**, R. 243). A mixture of the two naturally occurring asparagines has been produced by heating maleic anhydride to 110° with alcoholic ammonia (Ber. **29**, 2070).

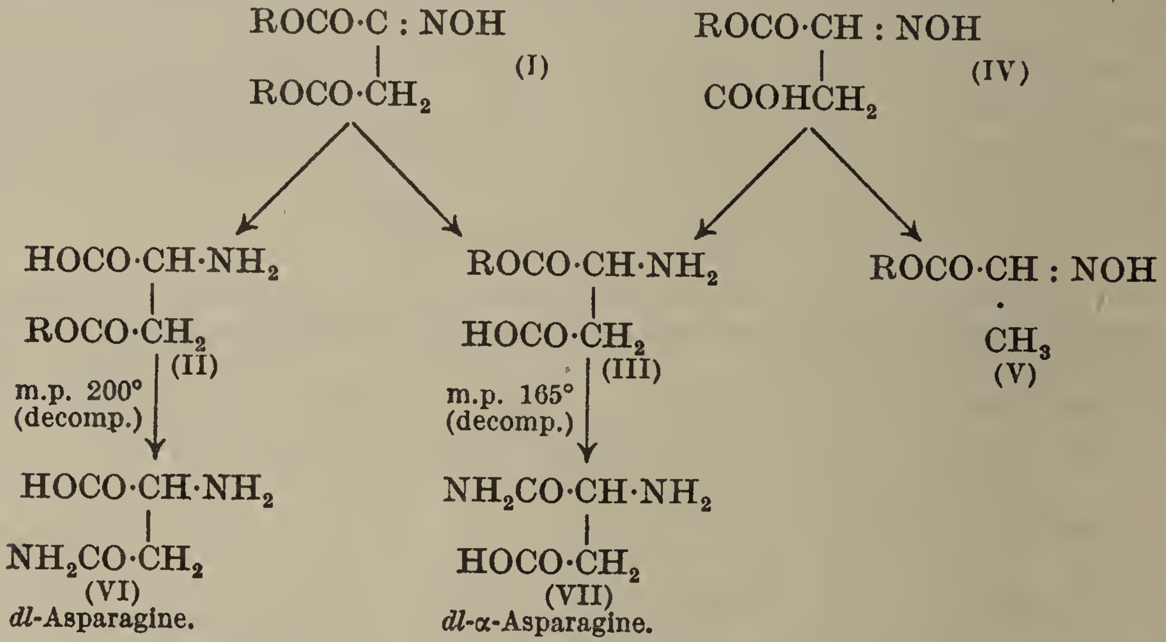
Both optically active asparagines crystallize in rhombic, right and left hemihedral crystals, which dissolve slowly in hot water, in alcohol and ether, but they are not easily soluble. It is not possible for them to combine in aqueous solution to an optically inactive asparagine. It is remarkable that the dextro-asparagine has a sweet taste, whilst the lævo-form possesses a disagreeable and cooling taste. Pasteur assumed that the nerve substance dealing with taste behaves towards the two asparagines like an optically active body, and hence reacts differently with each.

Similar differences of taste are observed with *d*- and *l*-valine (p. 444), *d*- and *l*-leucine (p. 444), and *d*- and *l*-serine (p. 596).

Constitution of the Asparagines.—When the oxime of oxaloacetic ester (I) is reduced by sodium amalgam, two isomeric ethyl hydrogen aminosuccinates (II) and (III) are formed, with partial hydrolysis. The constitution of the "α"-

compound (m.p. 165° (decomp.)) (III) is shown by its formation by reduction from the stereoisomeric ethyl hydrogen oximinosuccinates (IV) which yield α-oximinopropionic ester (V) by loss of CO_2. Hence it may be assumed that the ester, m.p. 200° (decomp.), contains the amino group in the β-position to the carbethoxy group (Ber. **22**, R. 241).

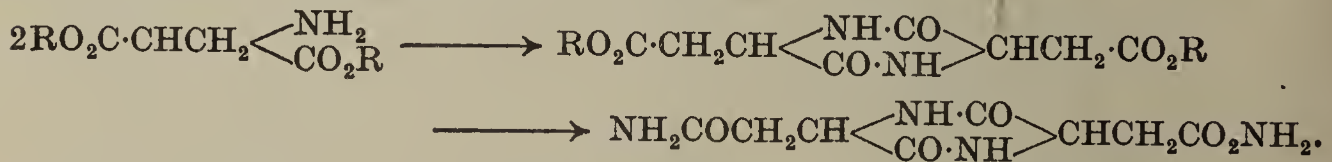
α-Asparagine (VII) is obtained from the α-ester by the action of ammonia, and inactive-β-(ordinary)-asparagine (VI) from the β-ester.



dl-α-Asparagine, iso*asparagine*, $HOCO{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CONH_2$, decomp. 214°, is formed from asparaginimide, diethyl aspartate and α-ethyl hydrogen aspartate by the action of ammonia; also from the potassium salt of aminofumaramic acid (p. 621) by the action of aluminium amalgam (C. 1897, I. 364).

Aspartic diamide, $NH_2CO{\cdot}CH(NH_2)CH_2CONH_2$, m.p. 131°, is prepared from aspartic ester and liquid ammonia. It is very soluble in water, and is easily decomposed.

Asparagine imide, *diketopiperazinediacetamide*, $(C_4H_6ON_2)_2$ (formula, see below), decomposes at 250°, is formed at the same time as asparagine diamide (above). It forms needles, and is with difficulty soluble in water. It is also prepared from bromosuccinic ester and ammonia; and from diketopiperazinediacetic esters (formula, see below); *methyl ester*, m.p. 248°, *ethyl ester*, m.p. 180–185°, by the same reagent. The latter ester is also obtained when aspartic ester is heated (Ber. **37**, 4599: **40**, 2059):

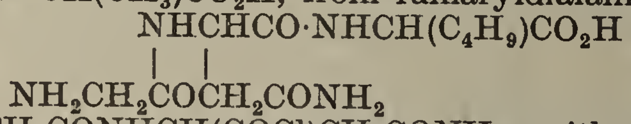


$$2RO_2C{\cdot}CHCH_2{<}{\begin{smallmatrix}NH_2\\CO_2R\end{smallmatrix}} \longrightarrow RO_2C{\cdot}CH_2CH{<}{\begin{smallmatrix}NH{\cdot}CO\\CO{\cdot}NH\end{smallmatrix}}{>}CHCH_2{\cdot}CO_2R$$

$$\longrightarrow NH_2COCH_2CH{<}{\begin{smallmatrix}NH{\cdot}CO\\CO{\cdot}NH\end{smallmatrix}}{>}CHCH_2CO_2NH_2.$$

Hydrolysis of the ester or amide results in the formation of diketopiperazinediacetic acid, and also the dipeptide. *Aspartylaspartic acid*, $HOOC{\cdot}CH_2CH(CO_2H)NHCOCH(NH_2)CH_2CO_2H$.

The *di-* and *tri-peptides* of the aspartic series are prepared in the same way as the peptides of the simple amino-acids (p. 445, etc.), and serine, cystine, etc. (pp. 596, 597), *e.g. glycylaspartic anhydride*, $\overline{NHCH_2CONHCH(CO})CH_2{\cdot}COOH$, from chloroacetyl aspartic ester; *leucylasparagine*, $C_4H_9{\cdot}CH(NH_2)CONHCH(CO_2H)CH_2CONH_2$, from bromo*iso*caproylasparagine; *aspartyldialanine*, $HO_2CCH(CH_3)NHCOCH_2CH(NH_2)CONHCH(CH_3)CO_2H$, from fumaryldialanine and ammonia; *glycylaspartylleucine*,



$$\begin{array}{l}NHCHCO{\cdot}NHCH(C_4H_9)CO_2H\\ |\quad|\\ NH_2CH_2COCH_2CONH_2\end{array}$$

from chloroacetylaspartyl chloride, $ClCH_2CONHCH(COCl)CH_2CONH_2$, with leucine ester and ammonia (Ber. **37**, 4585: **40**, 2048). *Hippurylaspartic acid*, $C_6H_5CO{\cdot}NHCH_2CONHCH(CO_2H)CH_2CO_2H$, is prepared from hippurazide (Vol. II) and aspartic acid, and yields a diazide, which, reacting with aspartic ester, gives rise to hippurylaspartylbis-aspartic ester, and still more complex chain compounds (J. pr. Chem. **70**, 158).

Homologues of Malic Acid

Malic acid homologues are formed: by the addition of hydrocyanic acid to β-ketonic esters; by the addition of HClO to alkylmaleic acids and subsequent reduction; and by the reduction of alkyloxaloacetic esters.

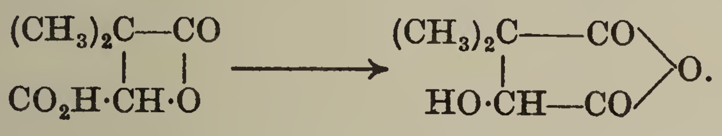
α-Hydroxypyrotartaric acid, citramalic acid, α-methylmalic acid, COOH·CH$_2$·C(OH)(CH$_3$)·COOH, m.p. 119°, is produced (1) by the oxidation of *iso*valeric acid (p. 304) with nitric acid; (2) from acetoacetic ester by means of HCN and HCl; (3) by the reduction of chlorocitramalic acid, the addition product resulting from the union of HClO with citraconic acid; (4) from methyl asparagine and nitrous acid. It breaks down at about 200° into water and citraconic anhydride (Ber. **25**, 196). Citramalic acid is resolved into its optical components by means of brucine (Ber. **32**, 712). *α-Methylmalic nitrile ester, acetoacetic ester cyanohydrin,* CH$_3$C(OH)(CN)CH$_2$CO$_2$C$_2$H$_5$, m.p. 8·5°, b.p. 127°/16 mm. (Ber. **39**, 1858).

α-Aminopyrotartaric acid, dl-*homoaspartic acid,* HO$_2$C·CH$_2$C(CH$_3$)(NH$_2$)CO$_2$H, m.p. 166°. Its diamide is formed from itaconic, citraconic, and mesaconic esters by the action of ammonia (Ber. **27**, R. 121). The acid is resolved into its *d*- and *l*- forms by crystallization. *Methylasparagine,* HO$_2$C·CH$_2$C(CH$_3$)(NH$_2$)·CONH$_2$ (?), m.p. 255° (decomp.), is formed from citraconic acid and ammonia (C. 1898, II. 762). *α-Anilinopyrotartaric acid,* HO$_2$C·CH$_2$C(CH$_3$)(NHC$_6$H$_5$)CO$_2$H, m.p. 135°, results from the hydrolysis of *α-anilinopyrotartaric monoester nitrile,* an oil, which is formed from acetoacetic ester cyanohydrin and aniline; also, from acetoacetic ester anil and hydrocyanic acid. *Ester amide,* m.p. 119°, is formed from the nitrile and sulphuric acid in the cold; it is easily converted into the *imide,* m.p. 168° (Ber. **35**, 2078).

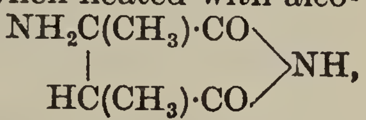
The anilinopyrotartaric acid when heated yields α-anilinopyrotartaric anil and citraconic anil (Ann. **261**, 138).

β-Methylmalic acid, COOH·CH(CH$_3$)·CHOH·COOH, is a colourless syrup, readily soluble in water, in alcohol, and in ether. It is formed when methyl oxaloacetic ester is reduced with sodium amalgam, and in an active *l*- form from a citraconic acid solution by the action of a mould (Ber. **27**, R. 470). Mesaconic acid and citraconic anhydride (Ber. **25**, 196, 1484) are produced when it is heated.

ββ-Dimethylmalic acid [2 : 2-dimethyl-3-butanol diacid], CO$_2$H·CH(OH)·C(CH$_3$)$_2$·CO$_2$H, m.p. 129°, is obtained by the action of alkalis or hydrochloric acid on the lactone. *ββ-Dimethylmalic lactone,* OCH(CO$_2$H)C(CH$_3$)$_2$CO, m.p. 46°, + *aq.*, m.p. 54°, is formed from monobromo-*as.*-dimethylsuccinic acid and silver oxide. It was the *first* β-lactone of the fatty acid series known (v. Baeyer and Villiger, Ber. **30**, 1954). When distilled under reduced pressure it is transformed into the *anhydride,* b.p. 145–150°/13 mm. (Ber. **33**, 3270):



αβ-Dimethylmalic acid, CH$_3$C(OH)(CO$_2$H)CH(CH$_3$)CO$_2$H, m.p. 143°, is prepared from α-methylacetoacetic ester cyanohydrin. During distillation it is converted into pyrocinchonic anhydride (p. 574). This, when heated with alcoholic ammonia, is converted into *aminodimethylsuccinimide,*



$$\begin{array}{l}NH_2C(CH_3)\cdot CO\\ \quad | \\ HC(CH_3)\cdot CO\end{array}\Big> NH,$$

m.p. 168° (Ber. **33**, 1410).

β-Ethylmalic acid, C$_2$H$_5$·CH(CO$_2$H)CH(OH)CO$_2$H, m.p. 87° (decomp.). Its *orthotrichloride,* γγγ-trichloro-β-hydroxy-α-ethylbutyric acid, CCl$_3$·CHOH·CHEt·COOH, m.p. 137°, is formed from chloral, ethylmalonic acid, and pyridine. When heated with potassium hydroxide it is changed into ethylmalic acid, which on heating decomposes into water and ethylmaleic acid (p. 573) (Ber. **38**, 2733).

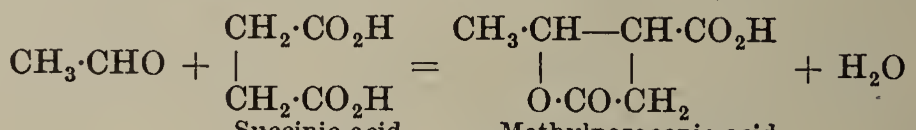
αβ-Methylethylmalic acid, m.p. 130° (Ber. **26**, R. 190).

Trimethylmalic acid, hydroxy-trimethylsuccinic acid, m.p. 155°, is obtained from dimethylacetoacetic ester with hydrocyanic acid, with subsequent hydrolysis by hydrochloric acid (Ber. **29**, 1543, 1619). The corresponding *β-lactone acid,* OC(CH$_3$)(CO$_2$H)·C(CH$_3$)$_2$CO, m.p. 119°, is obtained from bromo-trimethylsuccinic acid and silver oxide, similarly to the production of ββ-dimethylmalic acid lactone.

iso*Propylmalic acid*, m.p. 154°, from bromopimelic ester (Ann. **267**, 132).

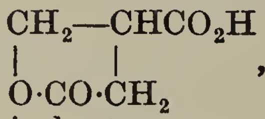
Paraconic Acids

Paraconic acids are γ-lactonic acids. Like the γ-hydroxyalkylhydroxymalonic acids, they are converted by alkalis and alkali earths into salts of the corresponding hydroxysuccinic acids (itamalic acids). When the latter are set free from their salts they immediately break down into water and lactonic acids. The alkylparaconic acids are formed when sodium succinate or pyrotartrate and aldehydes (acetaldehyde, chloral, propionic aldehyde) are condensed by means of acetic anhydride at 100–120° (Fittig, Ann. **255**, 1):



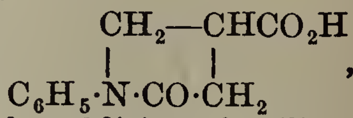
$$CH_3{\cdot}CHO + \begin{array}{l}CH_2{\cdot}CO_2H\\ |\\ CH_2{\cdot}CO_2H\end{array} = \begin{array}{l}CH_3{\cdot}CH{-}CH{\cdot}CO_2H\\ \quad|\qquad\ \ |\\ \ O{\cdot}CO{\cdot}CH_2\end{array} + H_2O$$

Succinic acid. Methylparaconic acid.



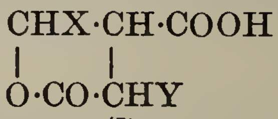
$$\begin{array}{l}CH_2{-}CHCO_2H\\ |\qquad\ |\\ O{\cdot}CO{\cdot}CH_2\end{array}$$

Paraconic acid, , m.p. 57°, is formed by the reduction of aconic acid (p. 616) and is best prepared by boiling itabromopyrotartaric acid with water and acidifying the calcium salt of the corresponding hydroxysuccinic acid —*itamalic acid*, formed on boiling itachloropyrotartaric acid with a soda solution. When boiled with bases, it forms salts of itamalic acid; it yields citraconic anhydride when it is distilled (Ann. **216**, 77: **255**, 10).



$$\begin{array}{l}\qquad\ \ CH_2{-}CHCO_2H\\ \qquad\quad|\qquad\ |\\ C_6H_5{\cdot}N{\cdot}CO{\cdot}CH_2\end{array}$$

pseudo*Itaconanilic acid, γ-anilidopyrotartrolactamic acid*, , m.p. 190°, is formed from itaconic acid (Ann. **254**, 129), by the addition of aniline, and subsequent lactam formation.



$$\begin{array}{l}CHX{\cdot}CH{\cdot}COOH\\ |\qquad\ |\\ O{\cdot}CO{\cdot}CHY\end{array}$$

(I)

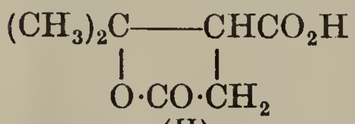
Methylparaconic acid [(I) above, X = Me, Y = H], m.p. 84·5°. *Ethyl ester*, b.p. 56°/17 mm., is also prepared from acetosuccinic ester by reduction with amalgamated aluminium. Sodium ethoxide solution transforms and hydrolyses it into methylitaconic acid. When distilled, methylparaconic acid yields valerolactone, ethylidenepropionic acid (p. 564), methylitaconic acid, and methylcitraconic acid (Ber. **23**, R. 91).

Trichloromethylparaconic acid [(I) above, X = CCl_3, Y = H], m.p. 97°, is changed by cold barium hydroxide solution into *iso*citric acid (*q.v.*). Reduction (C. 1897, II. 184; 1902, II. 343).

Ethylparaconic acid, [(I) above, X = Et, Y = H], m.p. 85°, when distilled, breaks up chiefly into carbon dioxide and caprolactone (p. 427). Hydrosorbic acid is formed at the same time (Ber. **23**, R. 93).

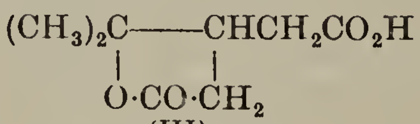
α-*Methylparaconic acid*, [(I) above, X = H, Y = Me], m.p. 104°, is obtained by the action of sodium amalgam on β-formylpyrotartaric ester, the reaction product of formic ester, pyrotartaric acid and sodium ethoxide. When heated it decomposes partly into water and pyrocinchonic anhydride (p. 574) (Ber. **37**, 1610).

αγ-*Dimethylparaconic acid*, [(I) above, X = Y = Me], m.p. 131°, b.p. 195°/14 mm., is formed by reducing β-acetopyrotartaric ester with sodium amalgam. When heated it partially breaks down into water and methylethylmaleic anhydride (p. 574), and into CO_2 and α-methyl-Δ^{β}-pentenoic acid, $CH_3{\cdot}CH:CH{\cdot}CHMe{\cdot}COOH$ (Ber. **37**, 1615).



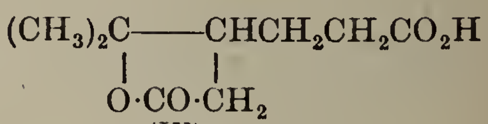
$$\begin{array}{l}(CH_3)_2C{-}CHCO_2H\\ \quad|\qquad\ |\\ \ O{\cdot}CO{\cdot}CH_2\end{array}$$

(II)



$$\begin{array}{l}(CH_3)_2C{-}CHCH_2CO_2H\\ \quad|\qquad\ |\\ \ O{\cdot}CO{\cdot}CH_2\end{array}$$

(III)



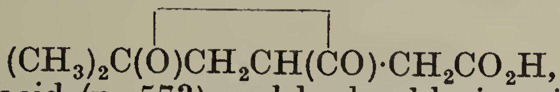
$$\begin{array}{l}(CH_3)_2C{-}CHCH_2CH_2CO_2H\\ \quad|\qquad\ |\\ \ O{\cdot}CO{\cdot}CH_2\end{array}$$

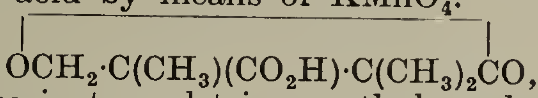
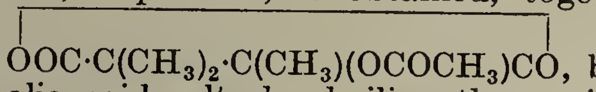
(IV)

Terebic acid (II), terpenylic acid (III), and homoterpenylic acid (IV), are three oxidation products of turpentine oil. They will be discussed in connection with pinene (Vol. II), the principal ingredient of the oil.

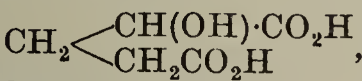
γ-Propylparaconic acid, [(I) above, X = C_3H_7, Y = H], m.p. 73·5°, yields, on distillation, γ-heptolactone (p. 427), heptylenic acid, $C_7H_{12}O_2$, and propylitaconic acid, $C_2H_{12}O_4$ (p. 573) (Ber. **20**, 3180).

γ-iso*Propylparaconic acid,* m.p. 69°, when distilled, decomposes into γ-*iso*-heptolactone and *iso*heptylenic acid.

iso*Propyl*iso*paraconic acid,*  $(CH_3)_2C(O)CH_2CH(CO){\cdot}CH_2CO_2H$, m.p. 143°, is formed from *iso*propylitaconic acid (p. 573) and hydrochloric acid at 130°, and by oxidation of *iso*butylsuccinic acid by means of $KMnO_4$.

ααβ-Trimethylparaconic acid,  $OCH_2{\cdot}C(CH_3)(CO_2H){\cdot}C(CH_3)_2CO$, m.p. 270°, is formed from sodium trimethylsuccinate and trioxymethylene, by the action of acetic anhydride. *Ethyl ester,* m.p. 34° ; *chloride,* m.p. 140° ; *amide,* m.p. 242°. The *anhydride,* m.p. 155°, is obtained, together with *trimethylacetylitamalic anhydride,*  $OOC{\cdot}C(CH_3)_2{\cdot}C(CH_3)(OCOCH_3)CO$, b.p. 185–195°/22 mm., from trimethylitamalic acid salts by boiling them with acetic anhydride (C. 1905, I. 1374).

Hydroxyglutaric Acid Group

α-Hydroxyglutaric acid,  $CH_2{<}\begin{array}{l}CH(OH){\cdot}CO_2H\\CH_2CO_2H\end{array}$, m.p. 72°, occurs in molasses. It is formed from α-bromoglutaric acid (C. 1902, II. 187) ; and by the action of nitrous acid on α-aminoglutaric acid. It also occurs in the reaction products of nitric acid on casein (C. 1902, II. 285). It crystallizes with difficulty (Ann. **208**, 66 : Ber. **15**, 1157). Its *lactone,* m.p. 50°, into which it readily passes when heated (Ann. **260**, 1129), is reduced to glutaric acid (p. 557) by hydriodic acid.

Glutaminic acid, *α-aminoglutaric acid,*  $CH_2{<}\begin{array}{l}CH(NH_2)CO_2H\\CH_2CO_2H\end{array}$, contains an asymmetric carbon atom (p. 37), and therefore can, like malic acid (p. 605), appear in three modifications.

dextrorotatory-Glutamic acid occurs in vetch and pumpkin seedlings, and with aspartic acid in beet molasses. It is formed together with other amino acids by the acid hydrolysis of proteins. Preparation, see Bull. Soc. Chim. [4] **27**, 750.

It forms brilliant rhombohedral crystals, m.p. 202° (decomp.), and is soluble in hot water but insoluble in alcohol and ether. *Hydrochloride,* $[\alpha]_D + 24{\cdot}44°$ is sparingly soluble.

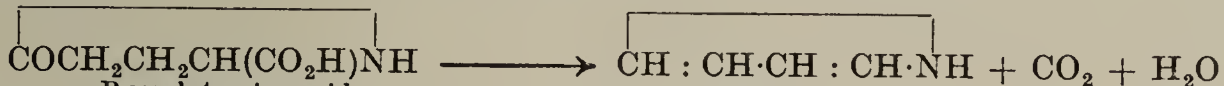
Ethyl ester, b.p. 140°/10 mm., is obtained from the acid by the action of alcohol and hydrogen chloride (Ber. **34**, 453). *Hydrochloride,* m.p. 96–98°. The action of nitrous acid leads to the formation of the weakly dextrorotatory diazoglutaric ester (J.A.C.S. **44**, 1798).

Polypeptides of glutamic acid, see Z. physiol. Chem. **105**, 58. *Glutathione* (p. 597) is an important tripeptide containing glutamic acid.

lævorotatory-Glutaminic acid is obtained from the inactive variety by means of *Penicillium glaucum* (p. 73).

Inactive-dl-*glutaminic acid,* m.p. 198°, results from ordinary glutaminic acid on heating it to 150–160° with barium hydroxide solution, and from α-*iso*nitrosoglutaric acid on reduction (Ann. **260**, 119). By repeated crystallization it can be resolved into *d*- and *l*-glutaminic acid (Ber. **27**, R. 269, 402 : **29**, 1700). Resolution is also effected by means of the strychnine salts of *r*-benzoylglutaminic acid (Ber. **32**, 2466).

dl-**Pyroglutaminic acid,** m.p. 182–183°, is the γ-lactam of the glutaminic acid, which results on heating ordinary glutaminic acid to 190°, and on continued heating breaks down into CO_2 and pyrrole (Ber. **15**, 1342) :



$$COCH_2CH_2CH(CO_2H)NH \longrightarrow CH : CH{\cdot}CH : CH{\cdot}NH + CO_2 + H_2O$$

Pyroglutamine acid. Pyrrole.

Glutamine, *α-aminoglutaramic acid,* $C_3H_5(NH_2)<\begin{matrix}CONH_2\\COOH\end{matrix}$, occurs together with asparagine in beet-root, in the seeds of pumpkins and other plants (Ber. **29,** 1882 : C. 1897, I. 105). Its optical rotation is not constant (Ber. **39,** 2932).

γ-Carbovalerolactonic acid, α-methylglutolactonic acid, valerolactone-γ-carboxylic acid, $O{\cdot}C(CH_3)(CO_2H)CH_2CH_2CO$, m.p. 68–70°, is deliquescent, and is produced (1) by oxidizing γ-*iso*caprolactone (p. 427) or *iso*caproic acid with nitric acid (Ann. **208,** 62 : Ber. **32,** 3661) ; and (2) by the action of potassium cyanide and hydrochloric acid on lævulinic acid.

γ-Carbovalerolactamic acid nitrile, α-methylpyrrolidone-α-carboxylic acid nitrile, $HNC(CH_3)(CN){\cdot}CH_2{\cdot}CH_2{\cdot}CO$, m.p. 141°, is formed from lævulinic ester, hydrocyanic acid, and alcoholic ammonia (*cf.* Ber. **38,** 1215).

iso*Propylglutolactonic acid,* $CO_2H{\cdot}C(C_3H_7)CH_2{\cdot}CH_2COO$, m.p. 67°, is prepared from α-dimethyllævulinic acid and hydrocyanic by means of hydrochloric acid (Ann. **288,** 185). *α-Hydroxy-γγ-dimethylglutolactonic acid,* $O{\cdot}CH(CO_2H){\cdot}CH_2C(CH_3)_2CO$, m.p. 85° (not sharp), results, together with dimethylglutaconic acid, when alcoholic potassium hydroxide acts on α-bromodimethylglutaric acid (C. 1902, I. 810 ; *cf.* also cyanodimethylacetoacetic ester, p. 624). *α-Hydroxy-βγ-dimethylglutolactonic acid, trans*-form, m.p. 142°, *cis*-form, liquid, b.p. 194°/15 mm., is formed from β-methyllævulinic acid, hydrocyanic and hydrochloric acids (C. 1900, II. 242). *α-Hydroxy-αγγ-trimethylglutolactonic acid,* $O{\cdot}C(CH_3)(CO_2H){\cdot}CH_2C(CH_3)_2CO$, m.p. 103°, is prepared from bromotrimethylglutaric acid and aqueous potassium hydroxide, and from mesitonic, hydrocyanic and hydrochloric acids (Ann. **293,** 220).

Mesitylic acid, *α-amino-αγγ-trimethylglutaric acid lactam,* $HNC(CH_3)(CO_2H)CH_2C(CH_3)_2CO$, m.p. 174°, is prepared by boiling the addition product of mesityl oxide and hydrochloric acid with potassium cyanide and alcohol (see Mesitonic acid, p. 479). If mesityl oxide alone be heated with two molecules of potassium cyanide in alcohol, there is formed on acidification *α-hydroxy-αγγ-trimethylglutaric acid dinitrile,* $NC{\cdot}C(CH_3)_2CH_2C(CH_3)(OH)CN$, m.p. 166°, which on being warmed with hydrochloric acid yields mesitylic acid (C. 1904, II. 1108). Oxidation with permanganate in acid solution yields *as.*-dimethylsuccinimide (Ber. **14,** 1074).

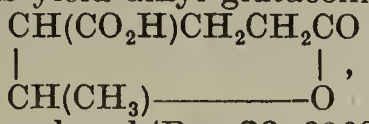
β-Hydroxyglutaric acid, $CH(OH)<\begin{matrix}CH_2CO_2H\\CH_2CO_2H\end{matrix}$, m.p. 95°, is obtained by the reduction of an aqueous solution of acetone dicarboxylic acid (Ber. **24,** 3250). It is decomposed on distillation into CO_2, H_2O and vinyl acetic acid (p. 345) ; Sulphuric acid and also boiling with aqueous alkali hydroxides (Ber. **33,** 1452) produce glutaconic acid (p. 575). Acetyl chloride gives rise to *acetoxyglutaric anhydride,* $CH_3COOCH(CH_2CO)_2O$, m.p. 88°. *Hydroxyglutaric dimethyl ester,* b.p. 150°/11 mm., yields acetoxyglutaric ester, which on distillation under ordinary pressures breaks down into glutaconic ester (Ber. **25,** 1976 : C. 1903, II. 1315). *β-Hydroxyglutaric diamide* is converted by sulphuric acid into glutaconimide. *β-Chloroglutaric acid* is obtained from glutaconic acid and hydrochloric acid. From it and from glutaconic acid ammonia produces *β-aminoglutaric acid.* $CO_2H{\cdot}CH_2CH(NH_2)CH_2CO_2H$, m.p. 248° (decomp.). *β-Bromoglutaric acid,* m.p. 139° (C. 1899, II. 28).

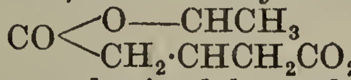
α-Amino-β-hydroxyglutaric acid, $COOH{\cdot}CH(NH_2){\cdot}CH(OH){\cdot}CH_2{\cdot}COOH$, was obtained by Dakin (Biochem. J. **12,** 290) by the hydrolysis of caseinogen and other proteins. It is dextrorotatory, crystallizes with difficulty. Synthesis of racemic form, see Biochem. J. **13,** 398.

sym.-*Dialkyl-β-hydroxyglutaric acids* are also formed by condensation of formic ester with α-bromo-fatty esters by means of zinc (see formation of secondary alcohols, p. 132) ; α-bromopropionic ester, α-bromobutyric acid and α-bromo-

*iso*butyric ester produce respectively αγ-dimethyl-, αγ-diethyl- and ααγγ-tetramethyl-β-hydroxyglutaric acids (C. 1898, II. 415, 885 : 1900, II. 529 : 1902, II. 107).

αα-Dimethyl-β-hydroxyglutaric acid, m.p. 169°, and *ααγ-trimethyl-β-hydroxyglutaric acid*, *cis*-form, m.p. 115° ; *trans*-form, m.p. 155°, are obtained from the corresponding di- and trimethyl acetone dicarboxylic esters (p. 624) (C. 1903, I. 76 : 1904, I. 720). *ααβ-Trimethyl-β-hydroxyglutaric ester* is prepared from α-dimethyl acetoacetic ester, bromoacetic ester, and zinc (C. 1903, II. 1315). The acetylated esters of these acids yield alkyl glutaconic acids when distilled.

δ-Caprolactone-γ-carboxylic acid,  $\begin{array}{l}CH(CO_2H)CH_2CH_2CO\\ |\qquad\qquad\qquad\qquad\quad |\\ CH(CH_3)\text{————}O\end{array}$, m.p. 197°, is formed when α-acetoglutaric acid (p. 624) is reduced (Ber. **29**, 2368). On dry distillation it yields γδ-hexenoic acid (p. 347) and α-ethylideneglutaric acid (p. 577).

γ-Valerolactone-β-acetic acid,  $CO\Big\langle\begin{array}{l}O\text{—}CHCH_3\\ CH_2\cdot CHCH_2CO_2H\end{array}$, m.p. 84° ; and *γ-heptolactone-β-acetic acid*, m.p. 88°, are obtained by reduction of the β-acylglutaric acids (p. 624), or their dilactones (Ann. **314**, 13).

HIGHER HYDROXY-DICARBOXYLIC ACIDS

α-Hydroxyadipic acid (Ber. **28**, R. 466). *α-Hydroxysebacic acid* (Ber. **27**, 1217).

α-Hydroxy-α-methyladipic acid, $CO_2H\cdot C(CH_3)(OH)\cdot[CH_2]_3CO_2H$, m.p. 92°, is prepared from γ-acetobutyric acid, potassium cyanide, and hydrochloric acid. On dry distillation it gives a mixture of γδ- and δε-hexenoic acids, which are characterized by their ability to be converted into γ- and δ-caprolactone (Ann. **313**, 371).

β-Hydroxy-β-methyladipic acid, $COOH\cdot CH_2C(CH_3)(OH)CH_2CH_2COOH$, and *β-Hydroxy-ααβ-trimethyladipic acid*, $CO_2H\cdot C(CH_3)_2C(CH_3)(OH)CH_2CH_2COOH$; their *lactone esters* are formed by condensation of bromoacetic ester and α-bromo*iso*butyric ester with lævulinic acid by means of zinc. The latter lactone ester is easily decomposed by alkalis into *iso*butyric acid and lævulinic acid (C. 1900, I. 1014 : Ber. **36**, 953).

α-Amino-adipic acid, $COOH\cdot CH(NH_2)CH_2CH_2CH_2CO_2H$, m.p. 206° (decomp.), is formed from α-oximino-adipic acid (p. 625) by reduction with tin and hydrochloric acid ; also by hydrolysis and decomposition of cyanopropylphthalimidomalonic ester, $C_6H_4(CO)_2NC(CO_2R)_2CH_2CH_2CH_2CN$, the product of reaction of sodium phthalimidomalonic ester and chlorobutyronitrile. It is sparingly soluble in water. When heated, it yields water and a *lactam*, *2-piperidone-5-carboxylic acid*, $\overline{NHCH(CO_2H)CH_2CH_2CH_2CO}$, m.p. 178°.

α-Amino-β-methyladipic acid is prepared from α-oximino-β-methyladipic acid. In the free state it immediately changes into its *lactam*, m.p. 144° (Ber. **38**, 1654 : C. 1903, II. 33).

α-Aminopimelic acid, $NH_2CH(COOH)[CH_2]_4COOH$, m.p. 225° (decomp.), is obtained from α-oximinopimelic acid.

B. UNSATURATED HYDROXYDICARBOXYLIC ACIDS

Mucolactonic acid, $\overline{OCOCH:CH\cdot C}HCH_2COOH$ (?), m.p. 122–125°, is obtained from hydromuconic dibromide and silver oxide.

The *aci-* or *enol*-forms of the *β-aldo-* and *β-keto-dicarboxylic acids* can also be included in this section ; *formyl-* and *acetyl-malonic acids* (pp. 615, 619), *formyl-* and *acetyl-succinic acids* (pp. 616, 622), *acetylglutaric acid* (p. 624), *oxaloacetic acid* (p. 619), *acetonedicarboxylic acid* (p. 623), *formyl-* and *acetyl-glutaconic acid* (p. 616), etc.

16. ALDODICARBOXYLIC ACIDS

A. β-Aldodicarboxylic Acids.

The simplest member, *Formylmalonic acid*, $OCH\cdot CH(CO_2H)_2$, is unknown in the free state. From its corresponding *aci-* or *enol*-form (see p. 453) are derived the following :—

Hydroxymethylenemalonic ester, $HOCH:C(CO_2C_2H_5)_2$, b.p. 218°, is formed as its *ethyl ether, ethoxymethylenemalonic ester*, $C_2H_5O{\cdot}CH : C(CO_2C_2H_5)_2$, b.p. 280°, from malonic ester and orthoformic ester by boiling with acetic anhydride and zinc chloride. The ethyl ether is hydrolysed by alcoholic potassium hydroxide into the potassium salt of hydroxymethylenemalonic ester. It can also easily unite with more malonic ester to form a dicarboxyglutaconic ester $(RO_2C)_2$-$CH{-}CH{=}C(CO_2R)_2$. This substance is decomposed by many reactions into derivatives of hydroxymethylenemalonic ester; ammonia produces *aminomethylenemalonic ester*, $H_2N{\cdot}CH : C(CO_2C_2H_5)_2$, m.p. 67°, which can be formed directly from ammonia and ethoxymethylenemalonic ester; hydrazine, hydroxylamine, and amidines give rise to cyclic derivatives of hydroxymethylenemalonic or formylmalonic acids (Ber. **26**, 2731 : **27**, 1658 : **30**, 821, 1083 : J.C.S. **59**, 746). *Copper salt*, m.p. 138°.

Formylsuccinic acid, $OCH{\cdot}CH(CO_2H)CH_2CO_2H$, is unknown in the free state. *Hydroxymethylenesuccinic ester*, aci-*formylsuccinic ester*, $HOCH : C(CO_2C_2H_5)$-$CH_2CO_2C_2H_5$, b.p. 125°/16 mm., is obtained from succinic ester, formic ester, and sodium ethoxide. With ferric chloride it produces a violet coloration. Reduction produces itamalic ester (p. 612), alkalis decompose it into succinic and formic acids (Ber. **26**, R. 91 : **27**, 3186. Action of Hydrazine, see Ber. **26**, 2061).

Aconic acid : aci-*formylsuccinic acid lactone*, $OCH : C(CO_2H)CH_2CO$, m.p. 164°, is formed when itadibromopyrotartaric acid is boiled with water; *methyl ester*, m.p. 85°. The acid yields formic and succinic acids when boiled with barium hydroxide; reduction produces paraconic acid (p. 612); phenylhydrazine gives the phenylhydrazone of β-formylpropionic hydrazide (p. 461) as well as CO_2; whilst with aconic methyl ester it forms the *phenylhydrazone* of *formylsuccinic monoester phenylhydrazide*, m.p. 167° (Ann. Spl. **1**, 347 : Ann. **329**, 373 : Ber. **31**, 2722).

Formylpyrotartaric ester (Ber. **37**, 1610).

α-Formylglutaconic acid, $OCH{\cdot}CH(CO_2H)CH : CHCO_2H$, is also a hypothetical acid, of which the following are derivatives :—

Coumalic acid, α-pyrone-3-carboxylic acid, α-aci-*formylglutaconic acid lactone*, $OCH : C(CO_2H)CH : CH{\cdot}CO$, m.p. 206° (decomp.), is formed from malic acid by heating it with concentrated sulphuric acid or with zinc chloride, with probably an intermediate formation of hydroxymethyleneacetic acid, $HOCH : CHCO_2H$ (p. 456), which, with the concentrated sulphuric acid, gives coumalic acid. This substance yields yellow salts with excess of alkali, like chelidonic and meconic acids (*q.v.*). Boiling with barium hydroxide solution decomposes it into formic and glutaconic acids; boiling with dilute sulphuric acid gives two molecules of CO_2 and crotonaldehyde. Ammonia produces the aci-*formylglutaconic acid lactam*, *-hydroxynicotinic acid*, $HN{\cdot}CH : C(CO_2H) : CH : CHCO$. Hydrazine causes decomposition of the lactazam of hydroxymethyleneacetic acid with formation of *pyrazolone* (p. 461) (Ann. **264**, 269 : Ber. **27**, 791). Methyl alcohol and hydrochloric acid cause fracture of the lactone ring and formation of *methoxymethyleneglutaconic ester*, $CH_3COCH : C(CO_2CH_3)CH : CHCO_2CH_3$, m.p. 62° (Ann. **273**, 164).

B. γ-**Aldodicarboxylic Acids.**

Acetalmalonic ester, $(C_2H_5O)_2CHCH_2(CO_2C_2H_5)_2$, b.p. 152°/15 mm., and *acetal methylmalonic ester* are prepared from sodium malonic ester and sodium methylmalonic ester with bromoacetal. The free acids lose water and form β-formyl fatty acids (p. 456).

17. KETONE-DICARBOXYLIC ACIDS

Dibasic carboxylic acids, containing a ketone group in addition to the carboxyl groups, are mostly synthesized as follows :—

1. By the introduction of acid radicals into malonic esters.
2. By introducing the residues of acid esters into acetoacetic ester.
3. By the condensation of oxalic esters with fatty acid esters.
4. By condensation of carboxylic anhydrides with tricarballylic acids.
5. From *sec.*-hydroxydicarboxylic acids or *tert.*-hydroxytricarboxylic acids by oxidation or decomposition.

These methods of formation will be more fully considered under the individual groups of the monoketone carboxylic acids. The position of the two carboxyl groups is again the basis for their classification, whereby the ketomalonic acid group, the ketosuccinic acid group, the ketoglutaric acid group, etc., are differentiated.

Ketomalonic Acid Group

Mesoxalic acid, *dihydroxymalonic acid,* [propanediol diacid], $(HO)_2C(COOH)_2$, m.p. 115°, like ordinary oxalic acid, glyoxylic acid, and other substances possessing adjacent CO groups, firmly holds a molecule of water, which is assumed to be present, not as water of crystallization, but to be combined with the CO-groups :

$(HO)_3C—C(OH)_3$	$(HO)_2CH—CO_2H$	$(HO)_2C=(CO_2H)_2$
Ortho-oxalic acid.	Orthoglyoxylic acid.	Orthomesoxalic acid.

Furthermore, esters of mesoxalic acid exist, derived from both forms, and are known as *keto-* (or *oxo-*) and *dihydroxy-malonic esters.*

Mesoxalic acid is prepared (1) from alloxan (p. 633) or mesoxalyl urea, an oxidation product of urea when boiled with barium hydroxide solution ; (2) from dibromomalonic acid, by boiling barium hydroxide solution, silver oxide, or aqueous sodium hydroxide (method of preparation : Ber. **35,** 1819) ; (3) from aminomalonic acid by oxidation with iodine in KI solution ; (4) from glycerol, by oxidation with nitric acid, sodium nitrate, and bismuth subnitrate (Ber. **27,** R. 666).

Mesoxalic acid crystallizes in deliquescent prisms. At higher temperatures it decomposes into CO_2 and glyoxylic acid, $CHO{\cdot}CO_2H$ (p. 455). It breaks up into CO and oxalic acid on the evaporation of its aqueous solution.

Mesoxalic acid behaves like a ketonic acid, inasmuch as it unites with primary alkali sulphites ; and when acted on by sodium amalgam in aqueous solution, it is changed to tartronic acid (p. 604). It combines with hydroxylamine and phenylhydrazine.

Salts.—Calcium mesoxalate, $C(OH)_2(CO_2)_2Ca$, and *barium mesoxalate,* are crystalline powders, not very soluble in water ; *ammonium salt,* $C(OH)_2{\cdot}(CO_2{\cdot}NH_4)_2$, crystallizes in needles ; *silver salt,* $C(OH)_2{\cdot}(CO_2Ag)_2$, when boiled with water yields mesoxalic acid, silver oxalate, silver, and CO_2 : *bismuth salt,* Ber. **27,** R. 667.

Esters.—Two series of esters may be derived from mesoxalic acid—the anhydrous or *ketomalonic esters,* $CO(CO_2R')_2$, and the *dihydroxymalonic esters,* $C(OH)_2(CO_2R')_2$. The keto- or oxo-malonic esters absorb water with avidity, and thereby change into their corresponding dihydroxymalonic esters. The two compounds bear the same relation to each other that chloral bears to chloral hydrate :

$$CCl_3{\cdot}CHO \quad \text{Chloral} \xrightarrow{H_2O} CCl_3{\cdot}CH(OH)_2 \quad \text{Chloral hydrate}$$

$$CO(CO_2C_2H_5)_2 \quad \text{Ketomalonic ester} \xrightarrow{H_2O} C(OH)_2(CO_2C_2H_5)_2 \quad \text{Dihydroxymalonic ester.}$$

During preparation a mixture of both forms is obtained if water is not excluded. Nevertheless, the hydrates easily pass into the anhydrous compounds when heated under reduced pressure.

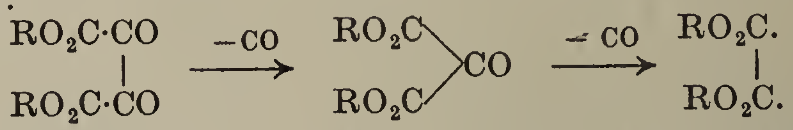
Mesoxalic ester is produced (1) from mesoxalic acid, by the usual methods ; (2) from *iso*nitrosomalonic ester (below) ; or from malonic ester direct by the action of nitrous gases (C. 1903, II. 658 : 1905, II. 120 : 1906, II. 320) :

$$2(RO_2C)_2CH_2 \xrightarrow{N_2O_3} 2(RO_2C)_2C : NOH \xrightarrow{N_2O_3} 2(RO_2C)_2C : O + 2N_2O + H_2O.$$

(3) From bromotartronic ester acetate or bromonitromalonic ester by the action of heat (Ber. **25**, 3614 : **37**, 1775) :

$$(RO_2C)_2C(OCOCH_3)Br \xrightarrow{-CH_3COBr} (RO_2C)_2CO \xleftarrow{-NOBr} BrNO_2C(CO_2R)_2.$$

(4) from dihydroxysuccinic ester when heated, some oxalic ester being also formed (Ber. **27**, 1305) :



Ketomalonic ethyl ester, $CO(CO_2C_2H_5)_2$, b.p. 101°/14 mm., $D_{16} = 1{\cdot}1358$, possesses a bright greenish-yellow colour. It is a mobile liquid, with a faint but not disagreeable odour.

Dihydroxymalonic methyl ester, $(HO)_2C(CO_2CH_3)_2$, m.p. 81°. *Dihydroxymalonic ethyl ester*, $C(OH)_2(CO_2C_2H_5)$, m.p. 57°, dissolves easily in water, alcohol, and ether.

Diethoxymalonic ester, $(C_2H_5O)_2C(CO_2C_2H_5)$, m.p. 43°, b.p. 225° (C. 1897, II. 569). *Diacetoxymalonic ester*, $(CH_3CO{\cdot}O)_2C(CO_2C_2H_5)_2$, m.p. 145°. *Dihaloidmalonic acids*, $X_2C(CO_2H)_2$ (see p. 544).

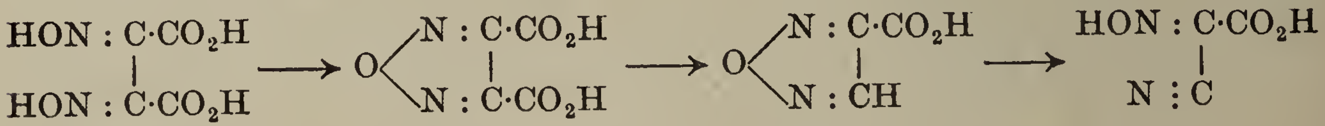
Nitrogen Derivatives of Mesoxalic Acid

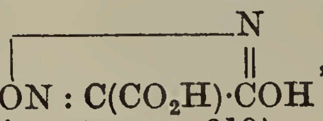
Nitrobromomalonic acid, $BrNO_2C(CO_2R)_2$; *methyl ester*, b.p. 133°/16 mm., and *ethyl ester*, b.p. 137°/11 mm., are formed from nitromalonic ester (p. 545) and bromine. As in other per-substituted nitromethanes (p. 186) the halogen is easily replaceable. Decomposition into ketomalonic ester (see above) (Ber. **37**, 1775).

Diaminomalonamide, $(NH_2)_2C(CONH_2)_2$, is prepared from dibromomalonic ester and ammonia. It consists of white crystals, and when heated, easily changes into *iminomalonamide*, $NH : C(CONH_2)_2$. *Tetramethyldiaminomalonic ester*, $[(CH_3)_2N]_2C(COOCH_3)_2$, m.p. 84°, is also obtained from dibromomalonic ester and $NH(CH_3)_2$. *Dianilinomalonic ester*, $(C_6H_5NH)_2C(COOCH_3)_2$, m.p. 125°, results from the action of aniline on dibromomalonic ester (Ber. **35**, 1374, 1813).

Oximinomesoxalic acid, iso*nitrosomalonic acid*, $HON{=}C(CO_2H)_2$, m.p. 126° (with decomposition into HNC, CO_2, and H_2O). It is formed when hydroxylamine acts on mesoxalic acid ; also from violuric acid, *iso*nitroso-malonyl-urea (p. 634) (Ber. **16**, 608, 1021) ; also from *iso*nitrosomalonic esters, $HON : C(CO_2R)_2$; *methyl ester*, m.p. 67°, b.p. 168°/16 mm., *ethyl ester*, b.p. 172°/12 mm., which are prepared from the malonic ester, sodium alcoholate, and alkyl nitrites. They form yellow alkali salts. *Amides* and *alkylamides* of *iso*nitrosomalonic acid (C. 1903, I. 441, 448).

Oximidomesoxalic nitrile ester, iso*nitrosocyanoacetic ester*, $HON : C(CN){\cdot}CO_2C_2H_5$, m.p. 128°, is formed from sodium cyanoacetic ester and amyl nitrite. It is a stronger acid than acetic acid (Ber. **24**, R. 595 : C. 1902, II. 1412). The free iso*nitrosocyanoacetic acid*, m.p. 129° (decomp.), has been obtained in different ways : (1) from dihydroxytartaric acid (*q.v.*) and hydroxylamine, some dioximinosuccinic acid being formed at the same time ; (2) from furazandicarboxylic acid, the anhydride of dioximinosuccinic acid ; (3) from furazanmonocarboxylic acid (p. 601) (Ber. **24**, 1988 : **28**, 72) :



(4) by the action of N_2O_3 on isoxazolonehydroxamic acid, prepared from oxaloacetic ester and 2 molecules of NH_2OH (see p. 622) (Ber. **28**, 761). Further derivatives of *iso*nitrosomalonic acid are : iso*nitrosocyanoacetamide*, desoxyfulminuric acid, $HON : C(CN)CONH_2$ (p. 296) : iso*nitrosocyanoacetohydroxamic acid*, $HON : C(CN)C\Big<{}^{OH}_{NOH}$, is prepared from formyl chloridoxime and NH_3 (pp. 289, 294). *Oxyfurazancarboxylic acid*, 

, is formed from hydroxyfurazanacetic acid (see **Oxaloacetic ester, p. 619**).

Phenylhydrazones.—The *phenylhydrazone* of mesoxalic acid, $C_6H_5NH{\cdot}N:C(COOH)_2$, m.p. 163° (decomp.), is obtained from the acid and phenylhydrazine or by the hydrolysis of the esters. The *methyl ester phenylhydrazone*, m.p. 62°, and *ethyl* derivative, an oil, are obtained from the mesoxalic esters and phenylhydrazine or by the action of benzenediazonium salts on sodiomalonic ester (Ber. **24**, 866, 1241 : **25**, 3183 : **28**, 858 : **37**, 4169). When hydrolysed they form the *monomethyl* and *monoethyl ester phenylhydrazones*, m.pp. 125° and 115°, and finally the phenylhydrazone of the acid.

Phenylhydrazonomesoxalic ester nitrile, benzeneazocyanoacetic ester, $C_6H_5NHN:C(CN)CO_2C_2H_5$, or $C_6H_5N:NCH(CN)CO_2C_2H_5$, m.p. 125°, is formed from sodium cyanoacetic ester and benzenediazonium chloride (Ber. **27**, R. 393 : **28**, R. 997 : C. 1906, II. 625) ; and also from potassium malonitrile and benzenediazonium salts. *Mesoxalic dinitrile phenylhydrazone*, $C_6H_5NHN:C(CN)_2$ (Ber. **29**, 1174). *Mesoxalic diamide phenylhydrazone*, m.p. 232° (Ber. **37**, 4173).

Mesoxalic diamide hydrazone, $NH_2N:C(CONH_2)_2$, m.p. 175°, is formed from dibromomalonic diamide and hydrazine (Ber. **28**, R. 1052).

Oxazomalonic acid is formed by the action of nitric oxide and sodium ethoxide on malonic ester. The product of reaction is unstable and forms a *sodium salt*, $N_2O:C(CO_2Na)_2 + 2H_2O$, with aqueous sodium hydroxide. This and other salts readily explode, especially when dry (Ber. **28**, 1795).

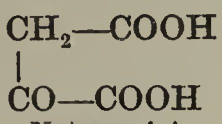
Acetylmalonic acid, $CH_3CO{\cdot}CH(CO_2H)_2$; *ethyl ester*, b.p. 150°/17 mm., results when sodium or, better, copper acetoacetic ester is acted on by chloroformic ester (p. 486) (Ber. **21**, 3567 : **22**, 2617). On hydrolysis it decomposes into CO_2, acetone and acetic acid. *Acetomalonic monoester anilide*, $CH_3CO{\cdot}CH(CONHC_6H_5)CO_2C_2H_5$, m.p. 58°, is formed by the union of acetoacetic ester and phenyl *iso*cyanate. It is decomposed by alkalis in the cold into acetic acid and malonic acid anilide (Ber. **33**, 2002).

Acetylcyanoacetic ester, cyanoacetoacetic ester, $CH_3CO{\cdot}CH(CN){\cdot}CO_2C_2H_5$, m.p. 56°, b.p. 119°/15–20 mm., is prepared (1) from the sodium or pyridine salt of cyanoacetic ester and acetyl chloride ; if acetic anhydride be employed, cyanoacetyl acetone is also formed ; (2) from dicyanoacetoacetic ester (p. 473) by separating hydrocyanic acid by alkalis. When the salts of cyanoacetoacetic ester are alkylated and acylated O-*derivatives* of the *enol*-form result : $CH_3C(OCH_3):C(CN)CO_2CH_3$, m.p. 97° ; $CH_3C(OCOCH_3):C(CN)CO_2CH_3$ and ammonia yield $CH_3C(NH_2):C(CN)CO_2CH_3$, m.p. 181° (C. 1904, I. 1135 ; Ber. **37**, 3384).

Propionyl cyanoacetic ester, b.p. 155–165°/50 mm. (Ber. **21**, R. 187, 354 : **22**, R. 407 : C. 1899, I. 185).

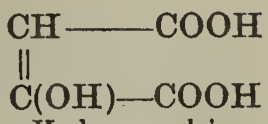
Ketosuccinic Acid Group

Oxaloacetic acid, *ketosuccinic acid* [butanone diacid], $C_4H_4O_5$, is relatively stable in the free state, and is simultaneously an α- and β-keto-acid. The acid is also tautomeric with hydroxymaleic and hydroxyfumaric acids :



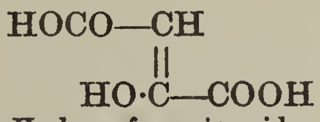
$$\begin{array}{l} CH_2\text{—}COOH \\ | \\ CO\text{—}COOH \end{array}$$

Ketosuccinic acid.



$$\begin{array}{l} CH\text{——}COOH \\ \| \\ C(OH)\text{—}COOH \end{array}$$

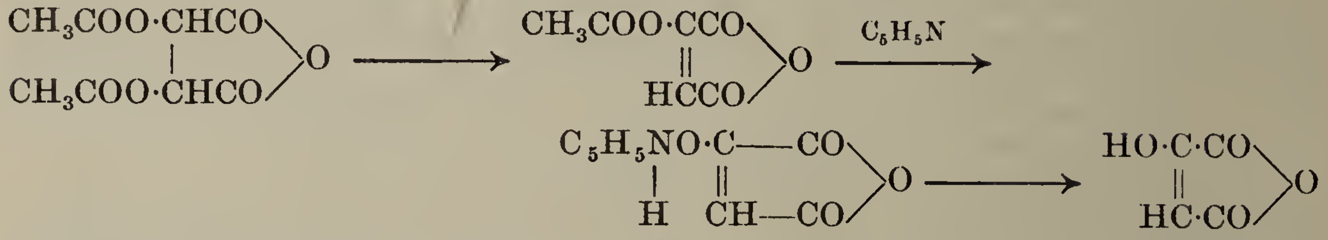
Hydroxymaleic acid.



$$\begin{array}{r} HOCO\text{—}CH \\ \| \\ HO{\cdot}C\text{—}COOH \end{array}$$

Hydroxyfumaric acid.

Oxaloacetic acid is prepared (1) from synthetic oxaloacetic esters (p. 620) by hydrolysis with concentrated hydrochloric acid in the cold (C. 1904, I. 85) ; (2) from malic acid (hydroxysuccinic acid) and permanganate or H_2O_2 and ferrous salts at a low temperature (C. 1900, I. 328 : 1901, I. 168) ; (3) from teraconic acid (*iso*propylidenesuccinic acid (p. 573) by cleavage of the chain with permanganate ; (4) from diacetyltartaric anhydride (*q.v.*) or acetoxymaleic anhydride (see below), pyridine and acetic acid, there is formed the pyridine salt of hydroxymaleic anhydride which with dilute acids yields oxaloacetic acid or hydroxymaleic acid (Ber. **40**, 2282):



$$\left.\begin{array}{l}CH_3COO\cdot CHCO\\ \quad\quad |\\ CH_3COO\cdot CHCO\end{array}\right>O \longrightarrow \left.\begin{array}{l}CH_3COO\cdot CCO\\ \quad\quad \|\\ \quad HCCO\end{array}\right>O \xrightarrow{C_5H_5N} \left.\begin{array}{l}C_5H_5NO\cdot C\text{---}CO\\ \ | \quad\ \|\\ \ H \quad CH\text{---}CO\end{array}\right>O \longrightarrow \left.\begin{array}{l}HO\cdot C\cdot CO\\ \quad\ \|\\ \ HC\cdot CO\end{array}\right>O$$

When the pyridine salt of hydroxymaleic anhydride is treated with 12% sulphuric acid, *hydroxymaleic acid*, m.p. 152°, is formed, which is converted by 30% acid into *hydroxyfumaric acid*, m.p. 184°, from the salts of which dilute acids regenerate hydroxymaleic acid; probably ketosuccinic acid is formed as an intermediate product. Hydroxyfumaric and hydroxymaleic acids show equally strong colorations with ferric chloride and decoloration of permanganate (reactions of the enol group). The heat of combustion of hydroxymaleic (286·58 cals.) is 10·8 cals. more than that of hydroxyfumaric acid (see Fumaric and Maleic acids, pp. 79, 569).

Hydroxymaleic anhydride, aci-*oxaloacetic anhydride*, $HO\cdot C_2H(CO)_2O$, m.p. 85° with transformation, is prepared from the pyridine salt, m.p. 108° (see above), by the action of HCl in ether. It is very hygroscopic. Acetyl chloride produces from it *acetoxymaleic anhydride*, $CH_3COO\cdot C_2H(CO_2)O$, m.p. 90°, which is also formed when oxaloacetic acid and acetylene dicarboxylic acid are acted on by acetic anhydride at 100° (Ber. **28**, 2511).

Hydroxymaleic anhydride, when treated with aniline at − 20° and acidified with 5*N* hydrochloric acid, is changed into *hydroxymaleinanilic acid*, $C_6H_5NH\cdot COC(OH):CHCOOH$, m.p. 113° (decomp.), which is converted by 10*N* sulphuric acid into *hydroxyfumaranilic acid*, m.p. 140° (decomp.). The *ethyl ester* of *oxaloacetanilic acid*, $C_6H_5NHCOCH_2CO\cdot CO_2C_2H_5$, m.p. 88°, the third isomer, is obtained from oxalic ester, acetanilide, and sodium ethoxide. The anil acids are converted by acetyl chloride into *hydroxymaleinanil* (and further into *acetoxymaleinanil*, $CH_3COO\cdot C_2H(CO)_2NC_6H_5$, m.p. 126°), which easily loses water and forms the dimolecular *xanthoxalanil*; aniline produces *anilinomaleinanil*, $C_6H_5NH\cdot C_2H(CO)NC_6H_5$, m.p. 233° (see above) (Ber. **40**, 2282).

Hydroxyfumaranilic acid and hydroxymaleinanilic acid, which are fairly stable alone, are decomposed even at 0° by aniline into CO_2 and pyroracemic anilide (p. 465).

Oxaloacetic ethyl ester, $C_2H_5OOC\cdot COCH_2COOC_2H_5$ or $C_2H_5OOC\cdot C(OH):CH\cdot COOC_2H_5$, b.p. 132°/24 mm., and the *methyl ester*, m.p. 77° (labile form, m.p. 87°), b.p. 137°/39 mm. (Ann. **277**, 375: Ber. **39**, 256), are formed from oxalic and acetic esters (p. 467) by means of sodium alcoholate (*W. Wislicenus*); also from acetylenedicarboxylic esters (p. 623) by the addition of water by warming with sulphuric acid; and from the silver salt of oxaloacetic acid and alkyl iodides. When boiled with alkalis, the ethyl ester undergoes " acid cleavage " into oxalic acid, acetic acid, and alcohol; when boiled with dilute sulphuric acid " ketone cleavage " occurs into CO_2 and pyroracemic acid, $CH_3\cdot CO\cdot CO_2H$ (p. 462). When heated under ordinary pressure it suffers " carbon monoxide cleavage " into CO and malonic ester, with pyroracemic ester as a by-product (Ber. **28**, 811):

$CO_2C_2H_5\cdot CO\cdot\boxed{CH_2CO_2C_2H_5}$ Acid cleavage
$CO_2C_2H_5\cdot CO\cdot CH_2\boxed{CO_2C_2H_5}$ Ketone cleavage
$CO_2C_2H_5\cdot\boxed{CO}\cdot CH_2CO_2C_2H_5$ Carbon monoxide cleavage.

Reduction converts oxaloacetic ester into the ester of *i*-malic acid (Ber. **24**, 3416).

Ferric chloride colours a solution of the ester a deep red. Copper acetate precipitates the ethyl ester as a green *copper salt* $(C_8H_{11}O_5)_2Cu + H_2O$, m.p. 155°, anhydrous, m.p. 163°. If this salt is boiled with methyl alcohol, it is converted into the copper salt of *oxaloacetic methyl ethyl ester*, $COOCH_3\cdot COCH_2COOC_2H_5$, b.p. 110°/13 mm. (Ann. **321**, 372).

Ammonia becomes added on to oxaloacetic ester, forming what is probably the *ammonium salt* of the aci-*oxaloacetic ester* (hydroxyfumaric or hydroxymaleic ester), $C_2H_5OOC\cdot C(ONH_4):CH\cdot COOC_2H_5$, m.p. 83°. It becomes gradually changed into oxalocitric lactone ester (p. 720), which is also formed from oxaloacetic ester and a tertiary amine (*cf.* Ber. **39**, 207).

Aminofumaric ester, $C_2H_5OCO\cdot C(NH_2):CH\cdot CO_2C_2H_5$, b.p. 142°/20 mm., is formed when the above ammonium salt is rapidly distilled; also, from chlorofumaric and chloromaleic ester and ammonia. Copper acetate slowly regenerates the copper oxaloacetic ester (Ann. **295**, 344). *Aminofumaramic ester*, m.p. 139°, and *aminomaleinamic ester*, m.p. 119° (C. 1897, I. 364).

Similarly to acetic ester, oxalic ester also condenses with acetonitrile (Ber. **25**, R. 175), and with acetanilide (see above) (Ber. **24**, 1245).

as.-*Diethoxysuccinic ester*, $CO_2C_2H_5\cdot C(OC_2H_5)_2CH_2CO_2C_2H_5$, is formed together with ethoxyfumaric ester (below) both from ordinary dibromosuccinic ester and acetylenedicarboxylic ester by the action of sodium ethoxide. *Diethoxysuccinic acid*, when allowed to stand under greatly reduced pressure or when heated to 100°, loses ether and becomes converted into oxaloacetic acid (Ber. **29**, 1792).

Ethoxyfumaric ester, $C_2H_5OOC\cdot C(OC_2H_5):CH\cdot COOC_2H_5$, b.p. 130°/11 mm., is prepared from silver oxaloacetic ester and iodoethane, and from dibromosuccinic ester, with simultaneous formation of diethoxysuccinic ester (see above), by taking up alcohol. The free *ethoxyfumaric acid*, m.p. 133°, is obtained from the ester by the action of cold dilute alkali. Acetic anhydride converts it into the fluid *ethoxymaleic anhydride*, which takes up water and forms *ethoxymaleic acid*, m.p. 126°. Both acids are hydrolysed by hydrochloric acid into oxaloacetic acid (Ber. **28**, 2512 : **29**, 1792).

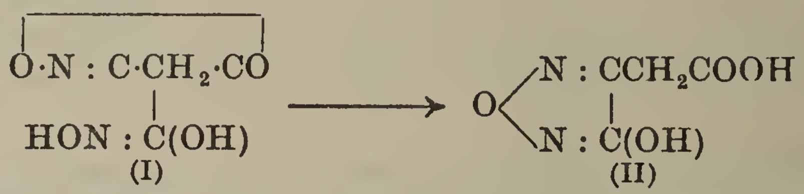
Methyloxaloacetic ester, oxalopropionic ester, $CO_2C_2H_5\cdot CO\cdot CH(CH_3)\cdot CO_2C_2H_5$, is formed from oxalic ester and propionic ester. *Methyloxaloacetanil*, $\overline{C}O\cdot CO\cdot CH(CH_3)CO\overline{N}C_6H_5$, m.p. 192°, is prepared from oxalic ester and propionanilide; also from *anilinocitraconanil*, $\overline{CO\cdot C(NHC_6H_5):C(CH_3)CON}C_6H_5$, the product of action of chloro- or bromo-citraconanil (p. 571) and aniline, by the action of sulphuric acid (Ber. **24**, 1256 : **35**, 1626).

Ethyloxaloacetic ester, oxalobutyric ester, $CO_2C_2H_5\cdot CO\cdot CH(C_2H_5)CO_2C_2H_5$ (Ber. **20**, 3394). *Dimethyloxaloacetic ester, oxalo*iso*butyric ester*, $CO_2C_2H_5\cdot CO\cdot C(CH_3)_2CO_2C_2H_5$, b.p. 117°/11 mm., is obtained from oxalic ester, bromo*iso*butyric ester, and magnesium (Ber. **41**, 964). *Methylethyloxaloacetic ester*, b.p. 134°/14 mm. (C. 1905, I. 1590).

Nitrogen Derivatives of Oxaloacetic Acid (Ber. 24, 1198). For the salt-like addition products of oxaloacetic anhydride and oxaloacetic ester with pyridine and ammonia, and their reaction products, see p. 620.

Oximes and Phenylhydrazones. α-*Oximinosuccinic acid*, m.p. 143° (decomp.), is formed from oxaloacetic acid and hydroxylamine. Acetic anhydride converts it into the β-*acid*, m.p. 126° (decomp.) (C. 1901, I. 353). β-*Oximinosuccinic monoethyl ester*, m.p. 54°, is prepared from the oxime of oxaloacetic ester and water; and α-*oximinosuccinic ethyl ester*, m.p. 107°, is obtained from di-*iso*-nitrososuccinylsuccinic ester and water. When heated they both yield CO_2 and α-oximinopropionic ester, $CH_3C:N(OH)CO_2C_2H_5$. Both monoesters are given the formula $CO_2H\cdot CH_2C:N(OH)CO_2C_2H_5$, and are assumed to be stereoisomers (Ber. **24**, 1204). *Oximinosuccinic ester*, $CO_2C_2H_5 \cdot C : N(OH) \cdot CH_2CO_2C_2H_5$, is a colourless oil (Ber. **21**, R. 351). See aspartic acid and asparagine (pp. 608, 609).

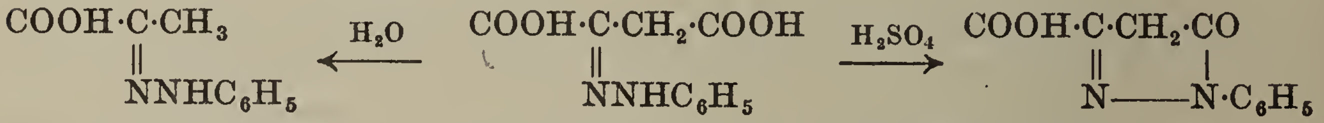
Hydroxylamine and ammonia act on oxaloacetic ester producing the ammonium salt of *isoxazolonehydroxamic acid* (I), which is converted by alkalis into *hydroxyfurazanacetic acid* (II).



$$\begin{array}{c}\text{O·N : C·CH}_2\text{·CO}\\ |\\ \text{HON : C(OH)}\\ \text{(I)}\end{array} \longrightarrow \text{O}\left\langle\begin{array}{l}\text{N : CCH}_2\text{COOH}\\ \quad |\\ \text{N : C(OH)}\\ \quad\text{(II)}\end{array}\right.$$

which is oxidized by permanganate into *hydroxyfurazancarboxylic acid* (Ber. **28**, 761).

Phenylhydrazine reacts with oxaloacetic acid to form a *phenylhydrazone*, $COOH \cdot C(NNH \cdot C_6H_5)CH_2 \cdot COOH$, m.p. 95°, with decomposition into CO_2 and pyroracemic acid phenylhydrazone. It undergoes the same decomposition when boiled with water, but when heated with acids, it forms phenylpyrazolonecarboxylic acid (C. 1902, II. 189):



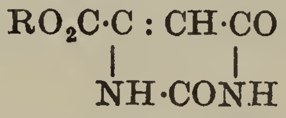
$$\begin{array}{l}\text{COOH·C·CH}_3\\ \quad\| \\ \quad\text{NNHC}_6\text{H}_5\end{array} \xleftarrow{H_2O} \begin{array}{l}\text{COOH·C·CH}_2\text{·COOH}\\ \quad\| \\ \quad\text{NNHC}_6\text{H}_5\end{array} \xrightarrow{H_2SO_4} \begin{array}{l}\text{COOH·C·CH}_2\text{·CO}\\ \quad\|\qquad\ | \\ \quad\text{N——N·C}_6\text{H}_5\end{array}$$

Phenylhydrazine becomes added to oxaloacetic ester like ammonia (p. 621); the *addition product*, m.p. 105°, is either a phenylhydrazine salt of hydroxyfumaric ester or is analogous to an aldehyde-ammonia compound. It readily changes into *oxaloacetic ester phenylhydrazone*, m.p. 97°, which is also formed from acetylene dicarboxylic ester and phenylhydrazine. The reaction products of hydrazine and phenylhydrazine on oxaloacetic acid also readily form pyrazolone derivatives by loss of alcohol (see above) (Ann. **246**, 320: Ber. **25**, 3442: **26**, 1721).

Diazosuccinic ester is formed when aspartic ester hydrochloride reacts with sodium nitrite: an optically active diazosuccinic ester is formed from an active aspartic ester (J.A.C.S. **44**, 1798). It is yellow in colour, and is easily decomposed. When boiled with water it forms fumaric ester; reduction re-produces aspartic ester. *Diazosuccinamic methyl ester*, $CH_3O_2C \cdot CN_2 \cdot CH_2CONH_2$, m.p. 81°, is formed, together with fumaramide, from diazosuccinic methyl ester and ammonia (Ber. **19**, 2460: **29**, 763: **37**, 1264).

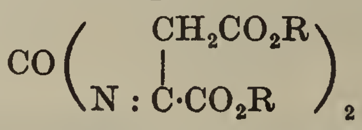
Urea unites with oxaloacetic ester to form *uracilcarboxylic ester* (1), m.p. 189°, and dioxaloacetic ester carbamide (2), m.p. 104°; guanidine produces *dioxaloacetic ester guanidine* (3), m.p. 147° (decomp.) (C. 1898, I. 445):

(1)



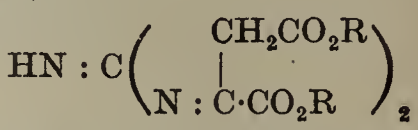
$$\begin{array}{l}\text{RO}_2\text{C·C : CH·CO}\\ \qquad\ |\qquad\quad |\\ \qquad\text{NH·CONH}\end{array}$$

(2)



$$\text{CO}\left(\begin{array}{l}\quad\text{CH}_2\text{CO}_2\text{R}\\ \quad |\\ \text{N : C·CO}_2\text{R}\end{array}\right)_2$$

(3)



$$\text{HN : C}\left(\begin{array}{l}\quad\text{CH}_2\text{CO}_2\text{R}\\ \quad |\\ \text{N : C·CO}_2\text{R}\end{array}\right)_2$$

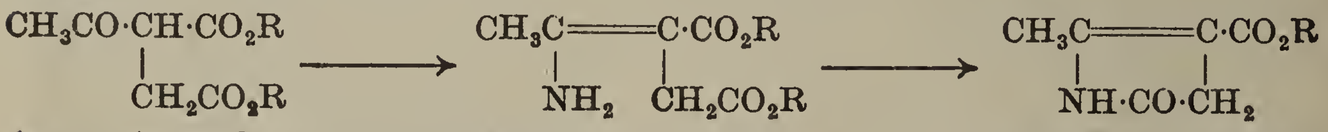
Acetosuccinic esters and **alkyl acetosuccinic esters** are produced when sodium acetoacetic esters and their monoalkyl derivatives are acted on by esters of the α-monohalogen fatty acids.

Acetosuccinic ester, $EtO \cdot CO \cdot CH_2 \cdot CH(COCH_3) \cdot COOEt$, b.p. 141°/14 mm., is prepared from sodium acetoacetic ester and bromo- or chloroacetic ester. The hydrogen atom of the CH-group, in the esters, can be replaced by alkyls, *e.g.*, by methyl:

α-Methylacetosuccinic ester, $CH_3COC(CH_3)(CO_2C_2H_5) \cdot CH_2CO_2C_2H_5$, b.p. 263°, is also formed from methyl acetoacetic ester and chloroacetic ester.

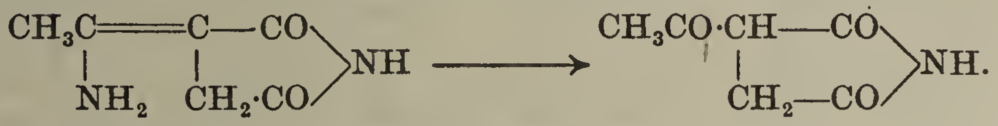
β-Methylacetosuccinic ester, $CH_3CO \cdot CH(CO_2C_2H_5) \cdot CH(CH_3)CO_2C_2H_5$, b.p. 263°, from acetoacetic ester and α-bromopropionic ester.

When heated alone the acetosuccinic acids act as in the *aci*- or *enol*-form, lose alcohol and form *olefinelactonecarboxylic acids* (C. 1898, I. 24). Ammonia and the primary amines produce *aminoethylidenesuccinic ester*, which readily changes into *olefine-lactam ester*:



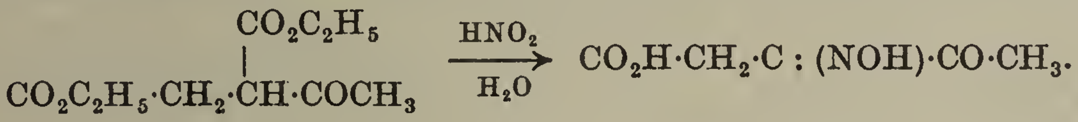
$$\begin{array}{l}\text{CH}_3\text{CO·CH·CO}_2\text{R}\\ \qquad\quad |\\ \qquad\text{CH}_2\text{CO}_2\text{R}\end{array} \longrightarrow \begin{array}{l}\text{CH}_3\text{C}\text{=\!=\!=}\text{C·CO}_2\text{R}\\ \quad |\qquad\ |\\ \text{NH}_2\ \ \text{CH}_2\text{CO}_2\text{R}\end{array} \longrightarrow \begin{array}{l}\text{CH}_3\text{C}\text{=\!=\!=\!=}\text{C·CO}_2\text{R}\\ \quad |\qquad\quad |\\ \text{NH·CO·CH}_2\end{array}$$

Ammonia produces *α-aminoethylidenesuccinic ester*, m.p. 72°, and *aminoethylidene* *succinimide,* which is converted by hydrochloric acid into *acetosuccinimide,* m.p. 84–87° (Ann. **260**, 137 : Ber. **20**, 3058 : C. 1897, I. 283) :



$$\left.\begin{array}{l}CH_3C{=\!=\!=}C{-}CO\\ \;\;|\qquad\quad\;|\\ NH_2\;\;\; CH_2\cdot CO\end{array}\right\rangle NH \longrightarrow \left.\begin{array}{l}CH_3CO\cdot CH{-\!-}CO\\ \qquad\qquad\;|\\ \qquad\quad\; CH_2{-\!-}CO\end{array}\right\rangle NH.$$

Acid cleavage changes acetosuccinic acids into acetic and succinic or alkyl succinic acids (pp. 300, 547). Ketone cleavage causes the formation of CO_2 and γ-keto-acids (p. 477). Nitrous acid causes acetosuccinic ester to lose alcohol and CO_2, and to change into *iso*nitrosolævulinic acid (p. 602) (*cf. iso*Nitrosoacetone, p. 407).



$$CO_2C_2H_5\cdot CH_2\cdot \overset{\overset{\displaystyle CO_2C_2H_5}{|}}{C}H\cdot COCH_3 \xrightarrow[H_2O]{HNO_2} CO_2H\cdot CH_2\cdot C:(NOH)\cdot CO\cdot CH_3.$$

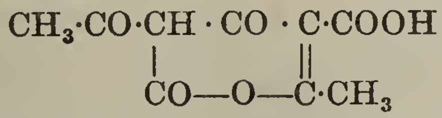
Ketoglutaric Acid Group

α-Ketoglutaric acid, $COOH\cdot CH_2CH_2\cdot CO\cdot COOH$, m.p. 113°, is obtained from oxalosuccinic ester by ketone cleavage (C. 1908, II. 786). *Cyanooximinobutyric acid,* $CO_2H\cdot CH_2\cdot CH_2\cdot C(:NOH)CN$, m.p. 87°, is a derivative of α-ketoglutaric acid. It is formed when cold sodium hydroxide acts on furazanpropionic acid (p. 601). When it is boiled with sodium hydroxide α-oximinoglutaric acid, $CO_2H\cdot CH_2\cdot CH_2C(:NOH)CO_2H$, m.p. 152°, is produced (Ann. **260**, 106).

Acetonedicarboxylic acid, *β-ketoglutaric acid,* $CO(CH_2CO_2H)_2$, m.p. about 130°, with decomposition into CO_2 and acetone. It may be obtained by warming citric acid with concentrated sulphuric acid (*v. Pechmann*, Ber. **17**, 2542 : **18**, R. 468 : Ann. **278**, 63 : large-scale preparation, see Ann. **422**, 5), and by oxidizing it with permanganate (C. 1900, I. 328). The diethyl ester may be prepared by the action of alcoholic hydrochloric acid on γ-cyanoacetoacetic ester.

Acetonedicarboxylic acid dissolves readily in water and ether. Decomposition into acetone and carbon dioxide which takes place on heating the acid alone, also occurs on boiling it with water, acids, or alkalis. The solutions of the acid yield a violet coloration with ferric chloride. The acid yields on reduction β-hydroxyglutaric acid (p. 614) and by the action of phosphorus pentachloride β-chloroglutaconic acid (p. 576).

The action of hydroxylamine produces the *oxime*, $COOH\cdot CH_2\cdot C(:NOH)\cdot CH_2\cdot COOH + H_2O$, m.p. 54° (*anhydrous*, m.p. 89°) (Ber. **23**, 3762). Nitrous acid produces di*iso*nitrosoacetone (p. 592) with elimination of carbon dioxide (Ber. **19**, 2466 : **21**, 2998). Acetic anhydride acts on the pure acid with the formation of the *anhydride,* m.p. 138–140° (Ann. **422**, 7) : from the crude acid, contaminated with traces of sulphuric acid, the reaction product with acetic anhydride is *dehydraceticcarboxylic acid* (I) (Ann. **273**, 186) :

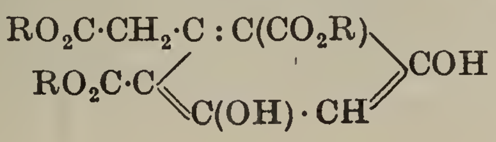


(I)

$$\begin{array}{l}CH_3\cdot CO\cdot CH\cdot CO\cdot C\cdot COOH\\ \qquad\qquad\quad|\qquad\quad\;\;\|\\ \qquad\qquad\; CO{-}O{-}C\cdot CH_3\end{array}\qquad(I)$$

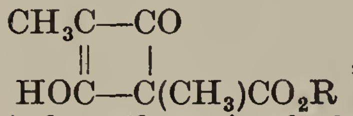
Esters of Acetonedicarboxylic Acid. Methyl ester, b.p. 128°/12 mm. *Ethyl ester,* b.p. 138°/12 mm. (Ber. **23**, 3762 : **24**, 4095 : C. 1906, II, 1395). *Ethyl hydrogen ester* is best obtained by the action of absolute alcohol on the anhydride of the acid : its *potassium* salt has been used in the synthesis of tropine (Ann. **422**, 11 : see Vol. II).

Acid and alkaline reagents cause the esters to lose alcohol and water, and readily to condense to orcinol-ω,2:6-tricarboxylic ester,



$$RO_2C\cdot C\left\langle\begin{array}{l}\!\!\!\!RO_2C\cdot CH_2\cdot C:C(CO_2R)\\ \\ C(OH)\cdot CH\end{array}\right\rangle COH \text{ (Vol. II).}$$

Sodium and alkyl iodides produce alkylacetonedicarboxylic esters, whereby the hydrogen atoms of the two CH_2-groups can be successively replaced by alkyl groups (Ber. **18**, 2289); it is, however, difficult to separate completely the various products of the reaction. *αα′-Dimethylacetonedicarboxylic ester*, $CH_3\cdot CH(CO_2R)COCH(CO_2R)CH_3$, is condensed by concentrated sulphuric acid into the ester of the monobasic aci-*dimethyl*cyclo*butanedionecarboxylic acid*,



$$\begin{array}{l} CH_3C\text{—}CO \\ \ \ \| \quad\ \ | \\ HOC\text{—}C(CH_3)CO_2R \end{array}$$

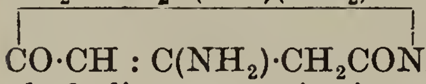
, (Ber. **40**, 1604), of which the sodium salt reacts with iodomethane in alcohol to form trimethylacetonedicarboxylic ester. This is also formed from αα-dimethylacetonedicarboxylic ester, $(CH_3)_2C(CO_2R)\cdot COCH_2CO_2R$, the product of reaction of dimethylmalonic ester, acetic ester, and sodium (C. 1903, I. 76: II. 190). *αα-Diethylacetonedicarboxylic ester*, $CO_2C_2H_5\cdot C(C_2H_5)_2\cdot COCH_2CO_2C_2H_5$, is formed by the carbon monoxide cleavage of α-diethyl-γ-oxalylacetoacetic ester, $C_2H_5O_2C\cdot C(C_2H_5)_2COCH_2COCO_2C_2H_5$ (*cf.* p. 620) (Ber. **33**, 3438).

Iodine and di-sodium acetonedicarboxylic ester produce hydroquinone tetracarboxylic ester (Vol. II).

Condensation of acetonedicarboxylic ester and aldehydes (Ber. **29**, 994: R. 93: **41**, 1692, etc.).

The O-*ethyl ether*, *β-ethoxyglutaconic ester*, $C_2H_5O_2C\cdot CH:C(OC_2H_5)\cdot CH_2CO_2\cdot C_2H_5$, b.p. 146°/14 mm., is formed from acetonedicarboxylic ester, orthoformic ester, and acetyl chloride. Hydrolysis produces at first the free *β-ethoxyglutaconic acid*, m.p. 182° (C. 1898, II. 414).

Aqueous ammonia converts the ester into *β-hydroxyaminoglutaminic ester*, $RO_2C\cdot CH_2C(OH)(NH_2)\cdot CH_2CONH_2$, and then *glutazine*, *β-aminoglutaconimide*,

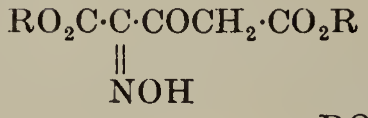


$$\overline{CO\cdot CH:C(NH_2)\cdot CH_2CONH}$$

, m.p. 300° (decomp.). The ester is converted by alcoholic ammonia into *β-aminoglutaconic ester*, $RO_2C\cdot CH:C(NH_2)CH_2CO_2R$ (Ber. **23**, 3762). Aniline at ordinary temperatures produces the *anil*, $C_6H_5N:C(CH_2CO_2R)_2$, m.p. 98°; whilst at 100° the *anilide*, $OC(CH_2CONHC_6H_5)_2$, is formed, together with other substances (Ber. **33**, 3442: **35**, 2081).

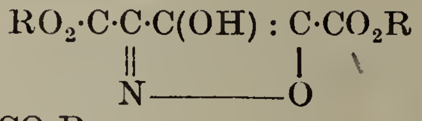
Nitrous acid converts acetonedicarboxylic esters into iso*nitrosoacetonedicarboxylic ester* (1) and *hydroxyisoxazoledicarboxylic ester* (2) (Ber. **24**, 857: see also Biochem. J. **25**, 1921); fuming nitric acid produces a *di*-iso*nitroso-peroxide* (3) (Ber. **26**, 997):

(1)



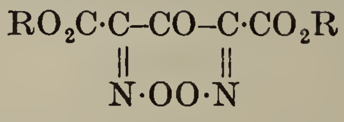
$$\begin{array}{l} RO_2C\cdot C\cdot COCH_2\cdot CO_2R \\ \qquad\quad \| \\ \qquad\ NOH \end{array}$$

(2)



$$\begin{array}{l} RO_2\cdot C\cdot C\cdot C(OH):C\cdot CO_2R \\ \qquad\quad \| \qquad\qquad\quad | \\ \qquad\ N\text{————}O \end{array}$$

(3)

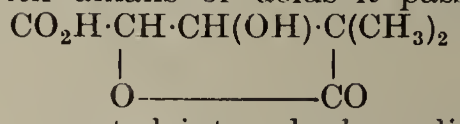


$$\begin{array}{l} RO_2C\cdot C\text{–}CO\text{–}C\cdot CO_2R \\ \qquad\quad \| \qquad\quad \| \\ \qquad\ N\cdot OO\cdot N \end{array}$$

The *phenylhydrazone* of *acetonedicarboxylic acid*, like its ester, readily forms the corresponding phenylpyrazoloneacetic acid (Ber. **24**, 3253):

$$\begin{array}{l} C_6H_5NHN:C\cdot CH_2CO_2H \\ \qquad\qquad\quad | \\ \quad HOOC\cdot CH_2 \end{array} \longrightarrow \begin{array}{l} C_6H_5N\cdot N:C\cdot CH_2CO_2H \\ \qquad\ \ | \qquad\ | \\ \qquad CO\text{—}CH_2 \end{array}$$

γ-Cyanoacetoacetic ester, $CN\cdot CH_2CO\cdot CH_2CO_2C_2H_5$, b.p. 135°/40 mm., is formed from γ-chloroacetoacetic ester and potassium cyanide (Ber. **24**, R. 18, 38). *γ-Cyanodimethylacetoacetic ester*, $CN\cdot CH_2CO\cdot C(CH_3)_2\cdot CO_2CH_3$, is formed from γ-bromodimethylacetoacetic ester. When heated with alkalis or acids it passes into *αα-dimethyl-βγ-dihydroxyglutaric acid lactone*,

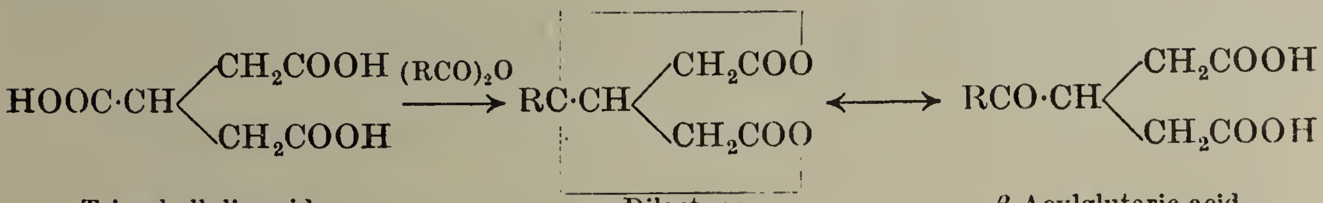


$$\begin{array}{l} CO_2H\cdot CH\cdot CH(OH)\cdot C(CH_3)_2 \\ \qquad\ | \qquad\qquad\qquad | \\ \qquad O\text{————}CO \end{array}$$

, m.p. 214° (Ber. **32**, 137), which, on reduction, is converted into γ-hydroxydimethylglutaric acid lactone (p. 614).

α-Acetyl-*n*-glutaric acids are prepared by the action of β-iodopropionic ester on the sodium compounds of acetoacetic ester, and the alkylacetoacetic esters: *α-acetoglutaric ester*, $RO_2C\cdot CH(COCH_3)CH_2\cdot CH_2\cdot CO_2R$, b.p. 272°; *α-ethyl-α-acetoglutaric ester*, $RO_2C\cdot C(C_2H_5)(COCH_3)\cdot CH_2CH_2CO_2R$, decomposes on distillation. On loss of CO_2, the free acids pass into the corresponding δ-keto-carboxylic acids (p. 480) (Ann. **268**, 113). With ammonia and primary amines they form lactams of δ-amino-olefine dicarboxylic mono-esters (Ber. **24**, R. 660).

β-Acylglutaric esters are formed when the sodium salt of tricarballylic acid (p. 647) is heated with carboxylic anhydrides, with simultaneous loss of CO_2; they are, however, converted at the temperature of reaction into *dilactones*, from which the ketone dicarboxylic acids are regenerated by the action of alkalis (*Fittig*, Ann. **341**, 1):



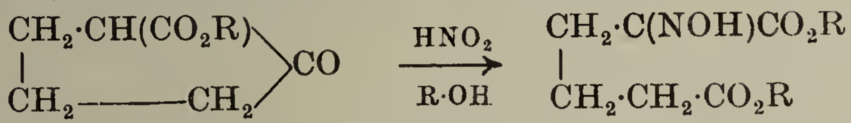
Tricarballylic acid. Dilactone. β-Acylglutaric acid.

β-Acetylglutaric acid, $CH_3CO \cdot CH(CH_2COOH)_2$, m.p. 58°, is obtained from its *dilactone*, m.p. 99°, b.p. 205°/12 mm., by the action of boiling water or alkalis. The dilactone is formed when sodium tricarballylate is heated with acetic anhydride at 120–130°, also when acetotricarballylic ester is boiled with hydrochloric acid (Ann. **295**, 94).

β-Butyryl- and *β-*iso*butyryl-glutaric acids*, $CH_3CH_2CH_2COCH(CH_2COOH)_2$, m.p. 88°, and $(CH_3)_2CHCOCH(CH_2COOH)_2$, m.p. 100° (decomp.); *dilactones*, m.pp. 55° and 90°, are obtained from sodium tricarballylate and butyric or *iso*butyric anhydrides.

HIGHER KETODICARBOXYLIC ACIDS

Oximes of α-keto-adipic acid and α-ketopimelic acid are obtained from adipic and pimelic esters by means of their carbocyclic condensation products (*cf.* p. 560) when acted on by ethyl nitrite and sodium alcoholate:



α-Oximinoadipic ester, m.p. 53°; *acid*, $HO_2C \cdot CH_2CH_2CH_2C(NOH)CO_2H$, m.p. 152° with decomposition into CO_2, H_2O, and glutaric acid nitrile (p. 558).

α-Oximino-γ-methyladipic ester, m.p. 50°; *acid*, $HOOC \cdot CH_2CH(CH_3) \cdot CH_2 \cdot C(NOH)CO_2H$, m.p. 163° with decomposition into CO_2, H_2O, and β-methyl glutaric acid nitrile (p. 558).

α-Oximinopimelic ester, an oil; acid, $HOOC[CH_2]_4C(NOH)CO_2H$, m.p. 143° with decomposition into CO_2, H_2O, and adipic acid nitrile (p. 561) (Ber. **33**, 579).

γ-Ketopimelic acid, acetonediacetic acid, hydrochelidonic acid, $CO(CH_2CH_2 \cdot CO_2H)_2$, m.p. 143°, is formed from chelidonic acid (or acetonedioxalic acid, p. 677) by reduction; also from furfuracrylic acid (Vol. III) by cleavage with hydrochloric acid. Treatment with acetyl chloride or acetic anhydride converts it into a *dilactone*, m.p. 75°, which when boiled with water or alkalis re-forms the acid:

This dilactone is also formed during the prolonged heating of succinic acid: $2C_4H_6O_4 = C_7H_8O_4 + CO_2 + 2H_2O$ (Ber. **24**, 143: Ann. **267**, 48: **294**, 165). Hydroxylamine produces the *oxime*, $C(NOH)(C_2H_4 \cdot CO_2H)_2$, m.p. 129° (decomp.); phenylhydrazine gives rise to the *phenylhydrazone*, $C(N_2H \cdot C_6H_5)(C_2H_4CO_2H)_2$, m.p. 107°. The *ethyl ester*, b.p. 171°/12 mm., gives, with bromine, sym.-*dibromoacetonediacetic ester*; *methyl ester*, m.p. 58°; *ethyl ester*, m.p. 49° (Ber. **37**, 3295).

Phoronic acid, γ-keto-ααεε-tetramethylpimelic acid, $CO[CH_2 \cdot C(CH_3)_2CO_2H]_2$, m.p. 184°, is formed from the addition product of phorone and two molecules of hydrochloric acid (p. 273) by successive treatments with potassium cyanide and hydrochloric acid (Ber. **26**, 1173). The corresponding *γ-dilactone*, m.p. 143° (Ann. **247**, 110).

δ-Keto-azelaic acid, acetonedi-β-propionic acid, $CO[CH_2CH_2CH_2CO_2H]_2$, m.p. 102° (*dimethyl ester*, m.p. 31°), is obtained from acetonedipropionic dicarboxylic ester, the product of di-sodium acetonedicarboxylic ester and two molecules of β-iodopropionic acid. Reduction changes it into *δ-hydroxyazelaic acid*, $HOCH[CH_2CH_2CH_2CO_2H]_2$, m.p. 105°. When heated it gives off water, but instead of a dilactone (p. 625) a hexamethylene ring body is formed: *dihydroresorcylpropionic acid*, $\overline{CO[CH_2]_3COC}H[CH_2]_2CO_2H$. This, on cleavage with nitrous acid (*cf.* p. 625), yields oximino-acetonedipropionic acid, $HO_2C[CH_2]_3COC(NOH)[CH_2]_2CO_2H$, which by the Beckmann inversion and hydrolysis of the product yields glutaric and succinic acids (Ber. **37**, 3816).

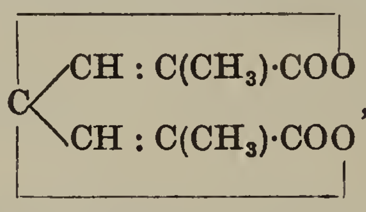
OLEFINE- AND DI-OLEFINE-KETONE DICARBOXYLIC ACIDS

Oxalocrotonic acid, $COOH{\cdot}CO{\cdot}CH_2CH:CH{\cdot}CO_2H$, melts at 190°, with formation of a di-olefine-lactone carboxylic acid, *α-pyrone-4-carboxylic acid*, $CO_2H{\cdot}\overline{C:CH{\cdot}CH:CHCOO}$, m.p. 228°; it is prepared from *oxalocrotonic ester*, $C_2H_5O_2C{\cdot}CO{\cdot}CH_2CH:CHCO_2R$, m.p. 79°, which is formed by condensation of oxalic and crotonic esters by sodium alcoholate. Like oxaloacetic ester, it possesses strong acidic properties (*cf.* Glutaconic ester, p. 454) (C. 1901, II. 1264).

α-Aceto-β-methylglutaconic acid, $CH_3CO{\cdot}CH(CO_2H)C(CH_3):CHCO_2H$, is the hypothetical acid of which the lactone of the aci-form is iso*dehydracetic acid, dimethylcoumalic acid*, $CH_3\overline{C:C(CO_2H){\cdot}C(CH_3):CHCO}$, m.p. 155°. This is obtained by condensation of acetoacetic ester by means of sulphuric acid; also by reaction of sodium acetoacetic ester with β-chlorocrotonic ester. The lactone decomposes at 205° into CO_2 and mesitene lactone (p. 454). *Methyl ester*, m.p. 67°, b.p. 167°/14 mm.; *ethyl ester*, m.p. 25°, b.p. 166°/12 mm., takes up two molecules of ammonia to form a salt which resembles ammonium carbonate in its decomposition products; at 100–140°, however, there is formed the corresponding *lactam*, $CH_3\overline{C:C(CO_2Et)C(CH_3):CHCONH}$, which is also formed by condensation of β-aminocrotonic ester (p. 454) (Ann. **259**, 172: Ber. **30**, 483).

β-Carbonyldiacrylic acid, $\Delta^{\alpha\delta}$-pentadien-γ-one-αε-dicarboxylic acid, $CO[CH:CHCOOH]_2$, m.p. above 230° (decomp.). Its esters are yellow-coloured; *dimethyl ester*, yellow leaflets, m.p. 169°, *diethyl ester*, yellow prisms, 50°, are formed from dibromoacetonediacetic esters (above) by the loss of 2 molecules of hydrobromic acid through quinoline (Ber. **37**, 3293).

Carbonyldimethacrylic acid, $\Delta^{\beta\epsilon}$-heptadien-δ-one-βζ-dicarboxylic acid, acetonedipyroracemic acid is precipitated from its salts in the form of its anhydride or γ-dilactone,

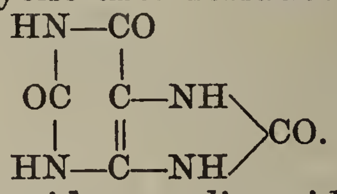


$$C\begin{cases}CH:C(CH_3){\cdot}COO\\ CH:C(CH_3){\cdot}COO\end{cases}$$

, m.p. 166°, b.p. 234°, which is obtained by the condensation of acetone and pyroracemic acid (Ber. **31**, 681).

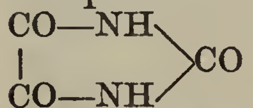
The Uric Acid Group

Uric acid is a compound of two cyclic urea residues combined with a nucleus of three carbon atoms:



$$\begin{array}{l}HN{-}CO\\ OC\quad C{-}NH\\ HN{-}C{-}NH\end{array}\Big>CO.$$

By its oxidation the ureides of two dicarboxylic acids—oxalic acid and mesoxalic acid—were made known. The ureide of a dicarboxylic acid is a compound of an acid radical with the residue, $NH{\cdot}CO{\cdot}NH$; *e.g.*

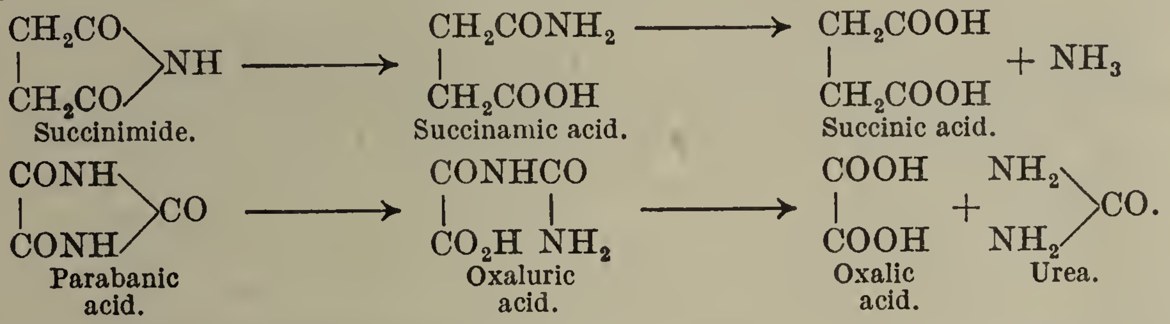


$$\begin{array}{l}CO{-}NH\\ CO{-}NH\end{array}\Big>CO$$

= ureide of oxalic acid, oxalyl urea, parabanic acid.

They are closely related to the imides of dibasic acids, succinimide

(p. 552), and phthalimide ; and parabanic acid may, for example, be regarded as a mixed cyclic imide of oxalic and carbonic acids. Like the imides, they possess the nature of an acid, and form salts by the replacement of the imide hydrogen with metals. The imides of dibasic acids are converted by alkalis and alkaline earths into amino-acid salts, which lose ammonia and become converted into salts of dibasic acids. Under similar conditions the ureide ring is ruptured. At first a so-called *-uric* acid is produced, which finally breaks down into its components, urea and a dibasic acid :



The urea derivatives of aldehydo- and keto-carboxylic acids, such as glyoxylic acid and acetoacetic acid, will be discussed in connection with the ureides and -uric acids of the dicarboxylic acids. Examples are allantoin and methyluracil. The first can also be prepared from uric acid, whilst methyluracil constitutes the parent substance for the synthesis of uric acid.

Ureides of Aldehyde- and Keto-monocarboxylic Acids

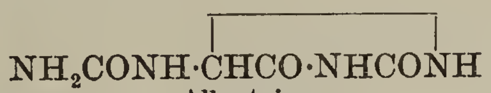
These bodies are connected themselves with the ureides of the oxyacids, hydantoin, and hydantoic acid, which have already been discussed (p. 499).

The following compounds with urea are derived from glyoxylic acid :

$$\underbrace{OCH\cdot CO\cdot NHCONH_2 \qquad HOCH\cdot CO\cdot NH\cdot CONH}$$

Allanturic acid or Glyoxalyl urea.

$(NH_2CONH)_2CHCOOH$
Allantoic acid.



$NH_2CONH\cdot CHCO\cdot NHCONH$
Allantoin.

Allantoin, $C_4H_6O_3$, m.p. 231° (decomp.), is present in the urine of sucking calves, in the allantoic liquid of cows, and in human urine after the ingestion of tannic acid. It has also been detected in beet-juice (Ber. **29**, 2652). It is produced artificially on heating glyoxylic acid (also mesoxalic acid, $CO(CO_2H)_2$) with urea to 100° ; also from hydantoin by the action of bromine and urea (Ann. **332**, 134).

Allantoin is formed by oxidizing uric acid with PbO_2 and MnO_2, potassium ferricyanide, or with alkaline $KMnO_4$ (Ber. **7**, 227). Methylated uric acids when oxidized in alkaline solutions yield methylallantoins (*cf.* p. 637) (Ann. **323**, 185).

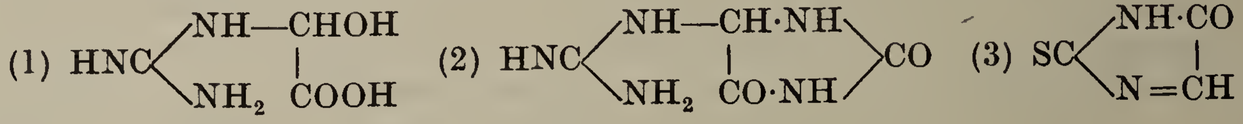
Allantoin crystallizes in glistening prisms, which are slightly soluble in cold water, but readily in hot water and in alcohol. It has a neutral reaction, but dissolves in alkalis, forming salts.

Sodium amalgam converts allantoin into glycoluril, or acetylenediurea.

Allantoic acid (formula, see above) decomposes at 165°, is prepared by hydrolysis of allantoin or its salts. It is not very soluble in water, and readily decomposes into urea and glyoxylic acid. *Ethyl ester*, $(NH_2CONH)_2CHCO_2$-C_2H_5, is prepared from glyoxylic ester, urea, and hydrochloric acid. Ammonia or alkali hydroxide solutions condense it to allantoin (C. 1904, I. 792 : 1906, II. 578).

Allanturic acid (formula, above) is obtained when allantoin is warmed with nitric acid, and by the oxidation of hydantoin (p. 499). It is a deliquescent amorphous mass, insoluble in alcohol.

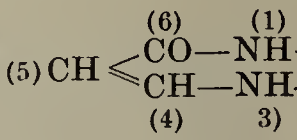
Glyoxylic acid unites with guanidine to form, according to the conditions of reaction, *guanidineglyoxylic acid* (1), m.p. 210° (decomp.), or *imidoallantoin* (2) (?) (Ann. **315**, 1); but with thiourea it forms *glyoxylthiocarbimide* (3), consisting of red-brown crystals (Ann. **317**, 151):



$$(1)\ HNC\left\langle\begin{matrix}NH-CHOH\\ \qquad\ |\\ NH_2\quad COOH\end{matrix}\right.\qquad (2)\ HNC\left\langle\begin{matrix}NH-CH\cdot NH\\ \qquad\ |\\ NH_2\quad CO\cdot NH\end{matrix}\right\rangle CO\qquad (3)\ SC\left\langle\begin{matrix}NH\cdot CO\\ \quad\ |\\ N=CH\end{matrix}\right.$$

Pyruvil, $NH_2CONH\cdot C(CH_3)CO\cdot NHCONH$, is formed by heating pyroracemic acid and urea, during which an intermediate product, $CH_3C(NHCONH_2)_2COOH$, is formed (C. 1901, II. 1114).

The **uracils** are the ureides of β-aldo- and β-keto-carboxylic acids. The simplest uracil, the ureide of formylacetic acid, its amino-derivative cytosine, like thymine, the ureide of α-formylpropionic acid, together with various purine derivatives (p. 637), occur in the nucleic acids (see Proteins) which occur in thymus glands, fish spermatozoa, yeast, kernels of plants, etc., and obtained from these by hydrolysis with sulphuric acid. The uracils contain the six-membered pyrimidine ring (Vol. III), which, when united to the five-membered glyoxaline ring, forms the skeleton of uric acid (*q.v.*). Derivatives of uracil are, therefore, employed in many ways for the synthesis of uric acid and other purine derivatives (pp. 639, *et seq.*).

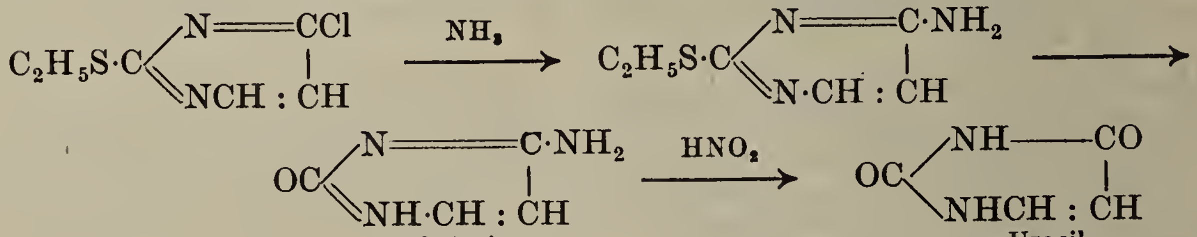
Uracil, 2 : 6-*dihydroxypyrimidine*, $C_4H_4O_2N_2$. 

$$(5)CH\left\langle\begin{matrix}\overset{(6)}{CO}-\overset{(1)}{NH}\\ \underset{(4)}{CH}-\underset{3)}{NH}\end{matrix}\right\rangle CO(2)$$

or $CH\left\langle\begin{matrix}C(OH):N\\ CH\text{——}N\end{matrix}\right\rangle C(OH)$, m.p. 335° (decomp.). It is prepared from nucleic acid (p. 748), and synthesized (1) from hydrouracil (p. 500) by bromination to bromohydrouracil, $C_4H_5BrO_2N_2$, and withdrawal of hydrobromic acid by means of pyridine; (2) Trichloropyrimidine, $C_4HCl_3N_2$, obtained from barbituric acid (p. 630), and $POCl_3$, reacts with sodium methoxide to form dimethoxychloropyrimidine, $C_4H(OCH_3)_2ClN_2$; this is reduced with zinc dust and hydrochloric acid to 2:6-dimethoxypyrimidine, $C_4H_2(OCH_3)_2N_2$, which is hydrolysed to uracil by evaporation with hydrochloric acids; (3) ψ-Methyl thiourea and formylacetic ester produce methyl mercapto-oxypyrimidine (*cf.* p. 510), which is decomposed by hydrochloric acid into methyl mercaptan and uracil (Ber. **34**, 3751 : **36**, 3379 : C. 1903, I. 1309).

Uracil is easily soluble in hot water, and with difficulty in alcohol and ether. It is precipitated by phosphotungstic acid and mercuric sulphate.

Cytosine, *uracilimide*, 2-*oxy*-6-*amino-pyrimidine*, $C_4H_5ON_3$ (see below), decomposed at 320–325°, is synthesized as follows: ethyl mercapto-oxypyrimidine (above) and PCl_5 give ethyl mercaptochloropyrimidine, which, by ammonia, is converted into ethyl mercapto-aminopyrimidine; this is decomposed by hydrobromic acid into mercaptan and cytosine (C. 1903, I. 1309). Nitrous acid converts cytosine into uracil (C. 1903, I. 1365):



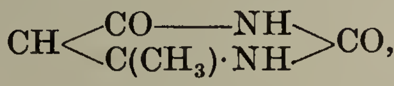
$$C_2H_5S\cdot C\left\langle\begin{matrix}N=CCl\\ |\\ NCH:CH\end{matrix}\right.\xrightarrow{NH_3}C_2H_5S\cdot C\left\langle\begin{matrix}N=C\cdot NH_2\\ |\\ N\cdot CH:CH\end{matrix}\right.\longrightarrow OC\left\langle\begin{matrix}N=C\cdot NH_2\\ |\\ NH\cdot CH:CH\end{matrix}\right.\xrightarrow{HNO_3}OC\left\langle\begin{matrix}NH-CO\\ |\\ NHCH:CH\end{matrix}\right.$$

Cytosine. Uracil.

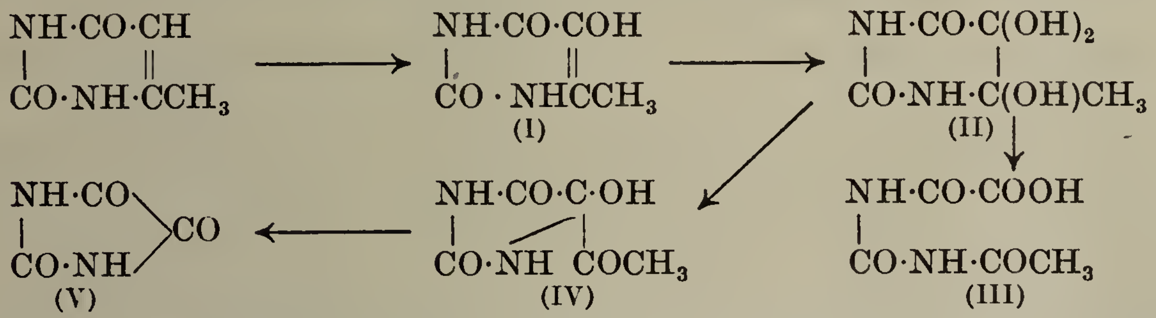
Cytosine is decomposed by permanganate into biuret (p. 502) and oxalic acid. It forms salts with nitric acid, sulphuric acid, H_2PtCl_6; also with silver, mercury, etc.; *picrate*, m.p. 278°. The isomeric 2-*amino*-6-*oxypyrimidine*, the guaneide of formylacetic acid, $NH_2C\left\langle\begin{matrix}NH\text{——}CO\\ |\\ NHCH:CH\end{matrix}\right.$, m.p. 276° (decomp.), is formed from guanidine and formylacetic ester.

Thymine, 5-*methyluracil*, $CH_3C\left\langle\begin{matrix}CO\cdot NH\\ CH\cdot NH\end{matrix}\right\rangle CO$, m.p. 318–321° (decomp.), is synthesized analogously to the uracils: (1) from 5-methylhydrouracil (p. 501);

(2) from *C*-methylbarbituric acid (p. 631) ; (3) from 2-methylmercapto-5-methyl-6-oxypyrimidine, the product of ψ-methyl thiourea and α-formylpropionic ester (Ber. **34**, 3751 : **38**, 3394 : C. 1903, I. 1309).

4-*Methyluracil*,  $CH{<}^{CO\text{———}NH}_{C(CH_3)\cdot NH}{>}CO$, m.p. 320° (decomp.), is synthesized : (1) from acetoacetic ester and urea and (2) from 4-methyl hydrouracil (p. 501) ; $POCl_3$ reacts with methyluracil and produces 4-methyl-2:6-dichloro-pyrimidine ; electrolytic reduction yields methyl trimethylene urea (p. 498) and αγ-diaminobutane.

Nitric acid and P_2O_5 give 5-nitro-4-methyluracil, and this on reduction forms aminomethyluracil (*cf.* p. 639). Permanganate produces 5-oxymethyluracil (I) and then 4 : 5 : 5-trioxymethylhydrouracil (II) (methyl *iso*dialuric acid). The latter, by further action of permanganate, is broken up into acetoxaluric acid (III) ; but alkalis produce acetylglyoxylurea (IV) (the ureide of αβ-diketobutyric acid) which, with chromic acid, yields parabanic acid (V) (p. 638).



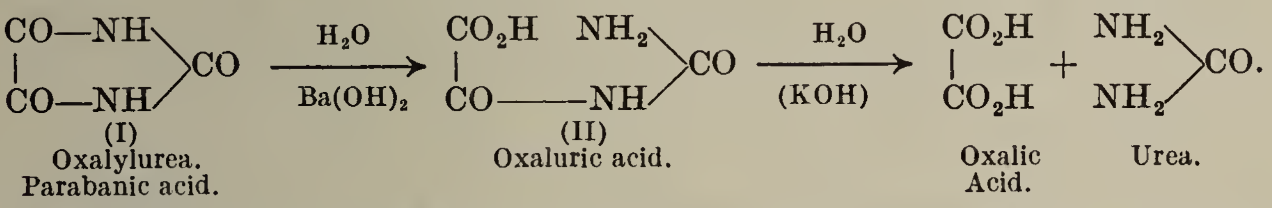
This series of oxidations and transformations probably represents the alkaline oxidation reactions of uric acid and its derivatives (*cf.* scheme, p. 638, and Ann. **333**, 144).

Methylation of 4-methyluracil by means of KOH and iodomethane produces 3 : 4-*dimethyluracil*, m.p. 22°, 1 : 4-*dimethyluracil*, m.p. 262°, and 1 : 3 : 4-*trimethyluracil*, m.p. 111° (Ann. **343**, 133, etc.).

Further uracil derivatives are obtained as intermediate compounds during the synthesis of uric acid (pp. 639–640).

Ureides or Carbamides of Dicarboxylic Acids

The most important members of this class are parabanic acid and alloxan. They were first obtained by oxidizing uric acid with nitric acid. When gently hydrolysed by acids or alkalis the ring is opened with the formation of a *-uric* acid of a dibasic acid, while more energetic alkaline hydrolysis forms urea and a dicarboxylic acid, *e.g.* :



Parabanic acid, *oxylylurea*, (formula (I) above), m.p. 243° (decomp.), is produced by the oxidation of uric acid and alloxan with ordinary nitric acid (Ann. **182**, 74), or better with perhydrol in acid solution (Ber. **59**, 721) ; by the treatment of hydantoin (p. 499) with bromine and water (Ann. **333**, 115) ; and, synthetically, by the action of $POCl_3$ on a mixture of urea and oxalic acid ; or by heating oxamide and diphenyl carbonate, $CO(OC_6H_5)_2$, together at 240° (C. 1900, I. 107). It is soluble in water and alcohol, but not in ether.

Its *salts* are easily converted by water into oxalurates ; silver salt, $C_3N_2O_3Ag_2$, is obtained as a crystalline precipitate.

Oxalylmethylurea, *methylparabanic acid*, m.p. 149·5°, is formed by boiling methyluric acid, or methylalloxan, with nitric acid, or by treating theobromine with chromic acid mixture. It is soluble in ether.

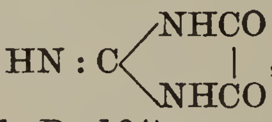
Oxalyldimethylurea, *dimethylparabanic acid*, *cholestrophane*, $C_3(CH_3)_2N_2O_3$, m.p. 145°, b.p. 276°, is obtained from dimethylalloxan and theine by oxidation, or by heating methyl iodide with silver parabanate.

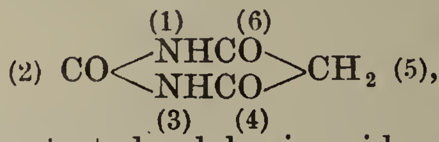
Oxaluric acid, $\mathrm{NH_2CO{\cdot}NHCO{\cdot}CO_2H}$, results from the action of alkali on parabanic acid. Free oxaluric acid is a crystalline powder, dissolving with difficulty. When boiled with alkalis or water it decomposes into urea and oxalic acid; heated to 200° with $\mathrm{POCl_3}$, it is again changed into parabanic acid.

The *ammonium salt,* $\mathrm{C_3H_3N_2O_4NH_4}$, and the *silver salt,* $\mathrm{C_3H_3N_2O_4Ag}$, crystallize in glistening needles.

The *ethyl ester,* $\mathrm{C_3H_3(C_2H_5)N_2O_4}$, m.p. 177°, is formed by the action of ethyl iodide on the silver salt, and has been synthetically prepared by allowing ethyl oxalyl chloride to act on urea.

Oxaluramide, oxalan, $\mathrm{NH_2CO{\cdot}NHCOCONH_2}$, is produced on heating ethyl oxalurate with ammonia, and by fusing urea with ethyl oxamate.

Oxalylguanidine,  $\mathrm{HN:C}\left\langle\begin{array}{l}\mathrm{NHCO}\\ \qquad\;|\\ \mathrm{NHCO}\end{array}\right.$, is formed from oxalic ester and guanidine (Ber. **26**, 2552: **27**, R. 164).

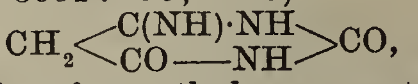
Malonylurea, *barbituric acid,*  $(2)\ \mathrm{CO}\left\langle\begin{array}{l}\overset{(1)}{\mathrm{NH}}\overset{(6)}{\mathrm{CO}}\\ \underset{(3)}{\mathrm{NH}}\underset{(4)}{\mathrm{CO}}\end{array}\right\rangle\mathrm{CH_2}\ (5)$, is obtained from alloxantin by heating it with concentrated sulphuric acid, and from dibromobarbituric acid by the action of sodium amalgam. It may be synthetically obtained by heating malonic acid and urea to 100° with $\mathrm{POCl_3}$, or by boiling urea and sodium malonic ester together in alcoholic solution (Ber. **37**, 3657).

It crystallizes with two molecules of water in large prisms from a hot solution, and when boiled with alkalis is decomposed into malonic acid and urea. Electrolytic reduction converts it into hydrouracil and trimethyleneurea (pp. 500, 498).

The hydrogen of $\mathrm{CH_2}$ in malonyl urea, as in malonic ester, can be readily replaced by bromine, $\mathrm{NO_2}$, and the *iso*nitroso-group. It forms metallic salts (Ber. **14**, 1643: **15**, 2846).

When silver nitrate is added to an ammoniacal solution of barbituric acid, a white *silver salt,* $\mathrm{C_4H_2Ag_2N_2O_3}$, is precipitated.

Malonyldimethylurea, 1 : 3-*dimethylbarbituric acid,* $\mathrm{CH_2[CON(CH_3)]_2CO}$, m.p. 123°, and *malonyldiethylurea,* m.p. 52°, are formed from malonic acid, $\mathrm{POCl_3}$, and the respective di-alkyl urea (Ber. **27**, 3084: **30**, 1815).

6-*Iminobarbituric acid,* 4-*aminouracil,*  $\mathrm{CH_2}\left\langle\begin{array}{l}\mathrm{C(NH){\cdot}NH}\\ \mathrm{CO{-\!\!-}NH}\end{array}\right\rangle\mathrm{CO}$, is obtained in the form of needles, which char on heating, from ethyl cyanoacetate, sodium ethoxide, and urea. During the reaction cyanoacetylurea, $\mathrm{CN{\cdot}CH_2CO{\cdot}NH{\cdot}CONH_2}$, is formed as an intermediate product, which can also be prepared from cyanoacetic acid, urea, and $\mathrm{POCl_3}$ or $\mathrm{(CH_3CO)_2O}$. 6-*Imino*-2-*thiobarbituric acid,* $\mathrm{CH_2[C_2O(NH)](NH_2)CS}$, is produced from cyanoacetic ester and thiourea; guanidine and this latter body form 2 : 6-*diiminobarbituric acid.*

These substances are decomposed by dilute acids into ammonia, barbituric acid, and 2-*thiobarbituric acid, malonylthiourea,* $\mathrm{CH_2(CONH)_2CS}$, and 2-*iminobarbituric acid, malonylguanidine,* $\mathrm{CH_2(CONH)_2C:NH}$, respectively. These compounds are directly produced from malonic ester and thiourea or guanidine (Ann. **340**, 312: Ber. **26**, 2553). 2 : 4 : 6-*Triiminobarbituric acid,* 2 : 4 : 6-*triaminopyrimidine,* $\mathrm{CH_2[C(NH){\cdot}NH]_2C:NH}$, is formed from malonic nitrile and guanidine (Ber. **37**, 4545). 2 : 4 : 6-*Trichloropyrimidine,* $\mathrm{CH\leqslant(C{\cdot}Cl{\cdot}N)_2\geqslant CCl}$, b.p. 213°, is formed from barbituric acid and $\mathrm{POCl_3}$ at 130–145° (Ber. **37**, 3657). It can be converted into uracil (p. 628).

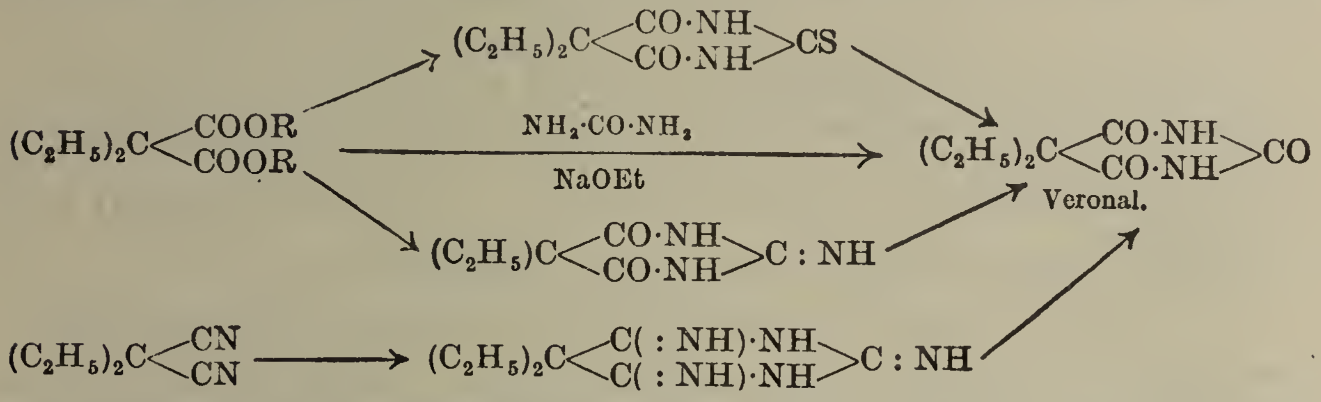
C- or 5 : 5-**Alkylated Barbituric Acids.**—These compounds have been minutely studied on account of some of their number acting as valuable soporifics, *e.g. C*-diethylbarbituric acid (*veronal*) and *C*-dipropylbarbituric acid.

Methods of formation. (1) Alkylation (by the action of iodomethane on the silver salt of barbituric acid) only produces directly *C*-dimethylbarbituric acid.

(2) Malonylguanidine (see above) is more conveniently alkylated, and the mono- and di-alkylmalonylguanidines which are produced are converted into mono- and di-alkylmalonylureas when heated with acid (C. 1906, II. 1465).

(3) By the condensation of mono- or dialkylmalonyl chlorides, or, better, mono- and dialkylmalonic esters, mono- and dialkylcyanoacetic esters or mono- and dialkylmalononitriles with urea, thiourea, guanidine or dicyanodiamide, with

or without the help of sodium alcoholate; *C*-alkylbarbituric acid or its thio- and imino-derivatives (see above) are formed: the latter, on hydrolysis, yield the barbituric acids. The dialkyl compounds produce the respective alkylbarbituric acids (Ann. **335**, 334: **340**, 310: **359**, 145: C. 1906, I. 514: II. 1465, 1695, etc.):



Preparation of 5 : 5-dialkylbarbituric acids with different radicals, see C. 1926, II, 2725.

Dialkylmalonuric acids, such as *diethylmalonuric acid*, $HOOC\cdot C(C_2H_5)_2\cdot CO\cdot NHCONH_2$, m.p. 162° (decomp.); *dipropylmalonuric acid*, m.p. 147° (decomp.), are formed from the malonic acid, urea, and fuming sulphuric acid. They readily decompose into CO_2 and dialkylacetourea; the *nitriles*, on the other hand, such as $NC\cdot C(C_2H_5)_2\cdot CO\cdot NHCONH_2$ (which is produced from alkylcyanoacetic esters, NaOR, and urea at ordinary temperatures) easily condense to cyclic compounds. Similarly, *diethylmalonyl diurethane*, $(C_2H_5)_2C(CONH\text{-}COOC_2H_5)_2$, is formed from diethylmalonyl chloride and two molecules of urethane; it is readily converted into diethylbarbituric acid by $C_2H_5\cdot ONa$ (C. 1906, II, 574).

5-*Methylbarbituric acid*, $CH_3CH(CONH)_2CO$, m.p. 203° (Ber. **38**, 3394). 5-*Ethylbarbituric acid*, m.p. 190°, unlike barbituric acid itself, is easily ethylated by iodoethane and alkalis to veronal. 5-*Propylbarbituric acid*, m.p. 208°. 5-iso*Propylbarbituric acid*, m.p. 216°.

5 : 5-*Dimethylbarbituric acid*, $(CH_3)_2C(CONH)_2CO$, m.p. 279°, is also obtained from dimethylmalonic acid, urea, and $POCl_3$; but if this treatment be applied to the homologues, only di-alkyl acetoureas, $R_2CHCO\cdot NHCONH_2$, are produced. This acid yields stable di-sodium salts, whilst the homologous dialkylbarbituric acids only give easily hydrolysed mono-sodium salts.

5 : 5-Diethylbarbituric acid, *veronal*, (Barbitonum), $(C_2H_5)_2C(CONH)_2CO$, m.p. 212°, has a bitter taste, and acts as a soporific. It crystallizes from hot water in the form of colourless spear-shape crystals, and is easily soluble in alkalis and ammonia. *Thioveronal, diethylmalonylthiourea*, $(C_2H_5)_2C(CONH)_2CS$, m.p. 180°, when heated with aniline and phenylhydrazine exchanges S for the groups $:NC_6H_5$ and $NNHC_6H_5$. Reduction with sodium amalgam produces di-ethyl malonamide, $(C_2H_5)_2C(CONH_2)_2$, *diethylmalonylmethylenediamide* or *desoxyveronal*, $(C_2H_5)_2C(CONH)_2CH_2$, m.p. 293°, and other substances (Ann. **359**, 154).

5 : 5-*Dipropylbarbituric acid*, m.p. 145°. For further homologues, see references given above.

5-*Phenyl*-5-*ethylbarbituric acid* is used as a drug, particularly in the treatment of epilepsy, under the name *luminal*.

Tartronylurea, *dialuric acid*, $CO<\begin{smallmatrix}NHCO\\NHCO\end{smallmatrix}>CH\cdot OH$, is formed by the reduction of mesoxalylurea (alloxan) with ammonium sulphide or with zinc and hydrochloric acid, and from dibromobarbituric acid by the action of hydrogen sulphide. On adding hydrocyanic acid and potassium carbonate to an aqueous solution of alloxan, potassium dialurate separates but potassium oxalurate remains dissolved:

$$2C_4H_2N_2O_4 + 2KOH = \underset{\text{Potassium dialurate.}}{C_4H_3KN_2O_4} + \underset{\text{Potassium oxalurate.}}{C_3H_3KN_2O_4} + CO_2.$$

iso*Dialuric acid*, isomeric with dialuric acid, is prepared from oxyuracil (p. 639) and bromine water; bases easily convert it into dialuric acid:

$$CO<\begin{smallmatrix}NH\cdot CH(OH)\\NH\cdot CO\end{smallmatrix}>CO \longrightarrow CO<\begin{smallmatrix}NH\cdot CO\\NH\cdot CO\end{smallmatrix}>CHOH.$$

Dialuric acid is differentiated from *iso*dialuric acid by its more ready oxidation (Ann. **315**, 246).

Dialuric acid crystallizes in needles or prisms, shows a very acid reaction, and forms salts with 1 and 2 equivalents of the metals (Ann. **344**, 1). It becomes red in colour in the air, absorbs oxygen and passes into alloxantin :

$$2C_4H_4N_2O_4 + O = C_8H_4N_4O_7 + 2H_2O.$$

Acetyldialuric acid, $CH_3COOCH(CONH)_2CO$ (?), m.p. 211°, is prepared from dialuric acid and acetic anhydride. It combines with alloxan to form acetylalloxantin.

Tartronyldimethylurea, $HOCH[CON(CH_3)]_2CO$, m.p. 170° (decomp.) (Ber. **27**, 3082).

Nitromalonylurea, *nitrobarbituric acid, dilituric acid* :

$\mathrm{CO}<{\mathrm{NHCO} \atop \mathrm{NHCO}}>\mathrm{CHNO_2}$, or $\mathrm{CO}<{\mathrm{NH{\cdot}CO} \atop \mathrm{NH{\cdot}CO}}>\mathrm{C:NOOH}$ (C. 1897, II. 266), is obtained by the action of fuming nitric acid on barbituric acid and by the oxidation of violuric acid (Ber. **16**, 1135). It crystallizes with three molecules of water and can exchange three hydrogen atoms for metals.

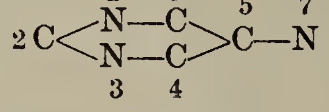
Nitromalonyldimethylurea, m.p. 148° (Ber. **28**, R. 321).

Aminomalonylurea, uramil, *aminobarbituric acid, dialuramide, murexan*, $\mathrm{CO}<{\mathrm{NHCO} \atop \mathrm{NHCO}}>\mathrm{CHNH_2}$, is obtained in the reduction of nitro- and *iso*nitrosobarbituric acid, and also alloxan phenylhydrazone with hydriodic acid ; by boiling thionuric acid with water, and by boiling alloxantin with an ammonium chloride solution. Alloxan remains in solution, whilst uramil crystallizes out. Uramil, together with alloxan, is formed in the decomposition of murexide and purpuric acid ; also, when ammonium dialurate is heated (Ann. **333**, 71). It is only slightly soluble in hot water, and crystallizes in colourless, shining needles, which redden on exposure to air.

Uramil dissolves in alkalis, forming salts, but prolonged action of alkalis causes decomposition into urea and aminomalonic acid, and other bodies (Ann. **333**, 77). When a solution of uramil is boiled with ammonia, murexide (p. 635) is formed. Nitric acid converts uramil into alloxan. Oxidation with permanganate (Ann. **333**, 91). *Acetyluramil*, $CH_3CO{\cdot}NHCH(CONH)_2CO$, is obtained from uramil and acetic anhydride ; its metallic salts form well-defined crystals.

Thionuric acid, *sulphaminobarbituric acid*, $HO_3S{\cdot}NH{\cdot}CH(CONH)_2CO$, and *alkylthionuric acids* are obtained as ammonium salts from alloxan or violuric acid (below) ; or from alkylated alloxans and ammonium sulphite ; or methyl ammonium sulphite. They are decomposed by acids into sulphuric acid and uramil or alkyl uramil. Dimethyl ammonium sulphite and alloxan yield a true bisulphite compound (see p. 633), which is decomposed into its components by acids (Ann. **333**, 93).

Alkyluramils.—In order to define the position of the alkyl groups the carbon and nitrogen atoms of uramil are numbered from 1 to 7, as is the uric acid (or purine) ring (p. 637) :



7-*Methyluramil*, $CO(NHCO)_2CH{\cdot}NHCH_3$; 1 : 3-*dimethyluramil*, $CO[N(CH_3){\cdot}CO]_2CHNH_2$; 1 : 3 : 7-*trimethyluramil* are obtained from the corresponding thionuric acids (see above) ; the 1 : 3-*dimethyluramil* is also produced by methylating uramil. *Dibarbiturylmethylamine*, $CH_3N[CH(CONH)_2CO]_2$, decomposes at 280°, is formed from alloxantin and methylamine hydrochloride (J. pr. Chem. [2] **73**, 473).

5-*Methyluramil*, $CO(NHCO)_2C(CH_3){\cdot}NH_2$, m.p. 237°, and 5-*ethyluramil*, m.p. 216°, are obtained from *C*-alkylbarbituric acids by bromination and the action of alcoholic ammonia (Ann. **335**, 359).

*pseudo***Uric acid,** *carbamidomalonylurea*, $\mathrm{CO}<{\mathrm{NH{\cdot}CO} \atop \mathrm{NH{\cdot}CO}}>\mathrm{CH{\cdot}NHCONH_2}$, is produced, as an ammonium salt, from uramil and urea at 180° ; as a potassium salt from uramil or murexide and potassium cyanate.

7-*Methyl*pseudo*uric acid* ; 1 : 3-*dimethyl*pseudo*uric acid* ; 1 : 3 : 7-*trimethyl-*

pseudo*uric acid* ; 1 : 3-*diethyl*pseudo*uric acid* are prepared from the corresponding alkyluramils and potassium cyanate. When heated with oxalic acid to 150°, or when boiled with hydrochloric acid, they change into the corresponding uric acids (Ber. **30**, 559, 1823).

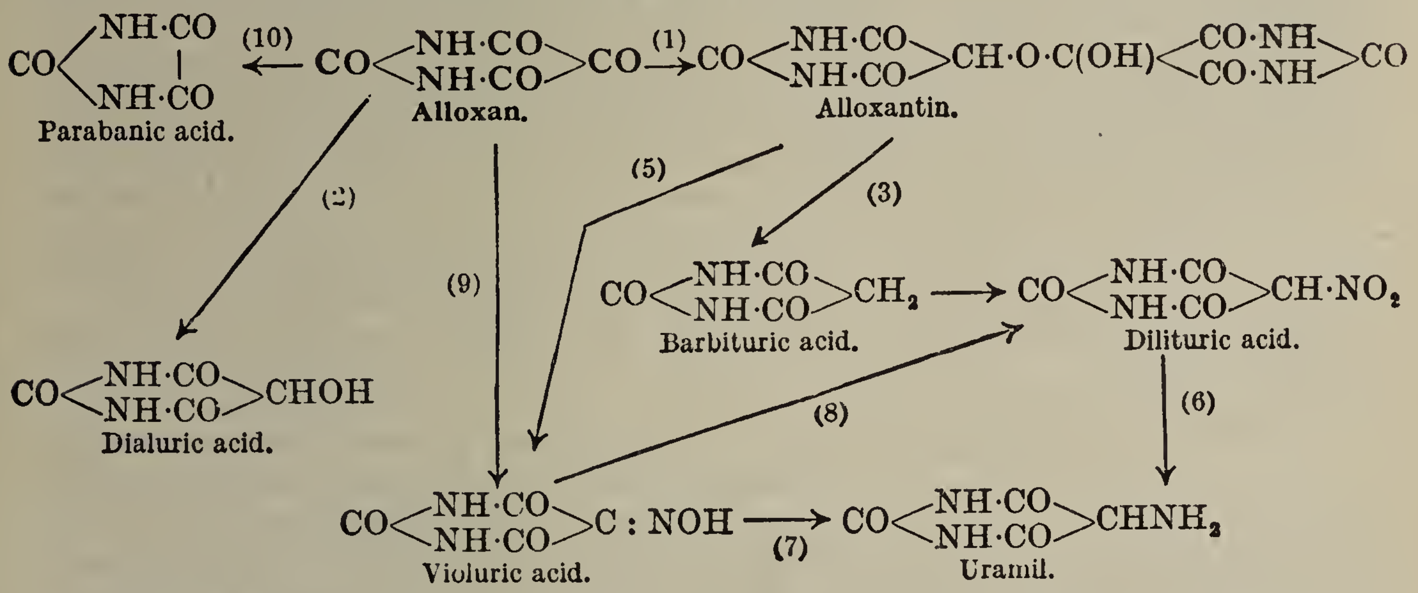
*Phenyl*pseudo*uric acid*, $(\mathrm{C_4H_3O_3})\cdot\mathrm{NHCONHC_6H_5}$, is prepared from uramil and phenyl *iso*cyanate (C. 1900, I. 806).

Thiouramil, $\mathrm{CO}\left<\begin{matrix}\mathrm{NH\cdot C(SH)}\\ \mathrm{NH\cdot CO}\end{matrix}\right>\mathrm{C\cdot NH_2}$, results when a solution of potassium urate is heated with ammonium sulphide to 155–160° (Ber. **28**, R. 909 : Ann. **288**, 157). It is a strong acid. Its solution imparts an orange colour to a pine chip. It gives the murexide test (p. 636). Nitric acid oxidizes it to sulphuric acid and alloxan. *β-Thio*pseudo*uric acid*, $\mathrm{CO}\left<\begin{matrix}\mathrm{NH\cdot C(SH)}\\ \mathrm{NHCO}\end{matrix}\right>\mathrm{C\cdot NHCO\cdot NH_2}$, is obtained from thiouramil and potassium cyanate (Ann. **288**, 171).

Alloxan, *mesoxalylurea*, $\mathrm{CO}\left<\begin{matrix}\mathrm{NH\cdot CO}\\ \mathrm{NH\cdot CO}\end{matrix}\right>\mathrm{CO}$, is produced by the careful oxidation of uric acid, or alloxantin, with nitric acid, chlorine, or bromine. Alloxan crystallizes from warm water in long, shining, rhombic prisms, with 4 molecules of $\mathrm{H_2O}$, the crystals having the formula : $\mathrm{CO(NHCO)_2C(OH)_2 + 3H_2O}$. When exposed to the air they effloresce with separation of $\mathrm{3H_2O}$. The last molecule of water is intimately combined (p. 617), as in mesoxalic acid, and does not escape until heated to 150°.

Alloxan is easily soluble in water, has a very acid reaction, and possesses a disagreeable taste. The solution placed on the skin slowly stains it a purple-red. Ferrous salts impart a deep indigo blue colour to the solution. When hydrocyanic acid and ammonia are added to the aqueous solution, the alloxan breaks down into $\mathrm{CO_2}$, dialuric acid, and oxaluramide (p. 630), which separates as a white precipitate (reaction for detection of alloxan).

Alloxan is the parent substance for the preparation of numerous derivatives (*Baeyer*, Ann. **127**, 1, 199 : **130**, 129), which have in part already received mention, and some of which will be discussed after alloxan. These genetic relationships are expressed in the following diagram :

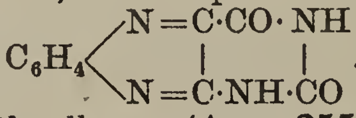


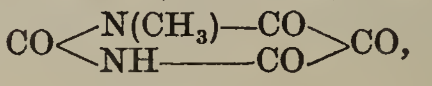
(1) Reducing agents, *e.g.* hydriodic acid, $\mathrm{SnCl_2}$, $\mathrm{H_2S}$, or Zn and hydrochloric acid, convert alloxan in the cold into *alloxantin* (p. 634) ; (2) on warming, into *dialuric acid* (p. 631). (3) Alloxantin digested with concentrated sulphuric acid becomes *barbituric acid* (p. 630) ; (4) fuming nitric acid changes it to *dilituric acid* ; (5) and with potassium nitrite it yields *violuric acid*. (6) (7) *Uramil* results from the reduction of dilituric acid and violuric acid. (8) *Dilituric acid* is formed when violuric acid is oxidized. (9) Hydroxylamine converts alloxan into its *oxime—violuric acid*. (10) Boiling dilute nitric acid oxidizes alloxan to *parabanic acid* and $\mathrm{CO_2}$.

The primary alkali sulphites unite with alloxan just as they do with mesoxalic acid, and crystalline compounds are obtained, *e.g.* $\mathrm{C_4H_2N_2O_4\cdot KHSO_3 + H_2O}$. Pure alloxan can be preserved without undergoing decomposition, but in the presence of small quantities of nitric acid it is converted into alloxantin. Alkalis or calcium or barium hydroxide change it to alloxanic acid, even when acting in the cold. Its aqueous solution undergoes a gradual decomposition (more rapid on heating) into alloxantin, parabanic acid, and CO_2.

Alloxan phenylhydrazone, m.p. 284° (Ber. **24**, 4140 : **31**, 1972).

Alloxan semicarbazide (Ber. **30**, 131).

Alloxan unites with aromatic amines to form dyes of quinonoid character (Vol. II) (Ann. **333**, 36 : J. pr. Chem. [2] **73**, 449). *o*-Phenylenediamine produces *alloxazine*,  $C_6H_4<\begin{array}{l}N{=}C{\cdot}CO{\cdot}NH\\ \quad\;\; | \qquad\quad |\\ N{=}C{\cdot}NH{\cdot}CO\end{array}$. Substances with an active CH_2-group readily react with alloxan (Ann. **255**, 230, etc.).

Methylalloxan,  $CO<\begin{array}{l}N(CH_3)—CO\\ NH——CO\end{array}>CO$, is produced by the oxidation of methyluric acid.

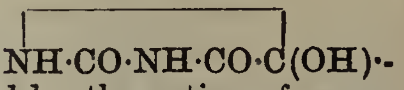
Dimethylalloxan, $CO[N(CH_3)\cdot CO]_2CO$, is produced when aqueous chlorine (from hydrochloric acid and $KClO_3$) acts on theine ; and by the careful oxidation of tetramethylalloxantin (Ber. **27**, 3082). When it is boiled with nitric acid, methyl- and dimethyl-parabanic acids are formed.

Diethylalloxan (Ber. **30**, 1814).

Dibromomalonylurea, dibromobarbituric acid, $Br_2C(CONH)_2CO$, results when bromine acts on barbituric acid, nitro-, amino- and *iso*nitroso-barbituric acids.

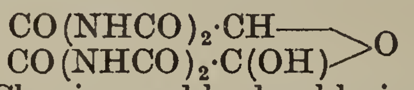
Oximinomalonylurea, iso*nitrosobarbituric acid, violuric acid*, $CO(NHCO)_2$-$C:NOH$, the oxime of alloxan, the first-known " ketoxime," is obtained by the action of potassium nitrite on barbituric acid, and of hydroxylamine on alloxan. It yields with metals blue, violet, or yellow coloured salts (Ber. **32**, 1723). When heated with the alkalis, it breaks down into urea and *iso*nitrosomalonic acid (p. 618).

Dimethylvioluric acid, m.p. 141° (Ber. **28**, 3142 : R. 912). *Diethylvioluric acid* (Ber. **30**, 1816).

Alloxanic acid, *5-hydroxyhydantoin-5-carboxylic acid*,  $\overline{NH\cdot CO\cdot NH\cdot CO\cdot C}(OH)\cdot$-$COOH$. The *barium salt*, $C_4H_2N_2O_5Ba + H_2O$, is formed by the action of warm baryta water on alloxan, a peculiar change from a six- to a five-membered ring taking place (Ann. **483**, 68). The free *acid* is obtained as a readily soluble crystalline mass by treating the barium salt with sulphuric acid ; it is a dibasic acid, the hydrogen of the 3-imino group being replaceable by metals, as well as that of the carboxyl group. Parabanic acid is formed on oxidation, and by reduction with hydriodic acid, hydantoin is produced (Ann. **119**, 127 : **130**, 159).

Diureides.—When the ureides, parabanic acid, alloxan and dimethylalloxan are reduced, there is probably combination of the reduced with the still unreduced molecules (see Vol. II, Quinhydrone), whereby the diureides, oxalantin, alloxantin and amalic acid are formed (*cf.* Ann. **333**, 63 : **344**, 17).

Oxalantin, *leucoturic acid*, $C_6H_6N_4O_6$, is obtained by the reduction of parabanic acid.

Alloxantin,  $\begin{array}{l}CO(NHCO)_2\cdot CH——\\ CO(NHCO)_2\cdot C(OH)\end{array}>O + 3H_2O$, is obtained (1) by reducing alloxan with $SnCl_2$, zinc and hydrochloric acid, or H_2S in the cold ; (2) by mixing solutions of alloxan and dialuric acid ; (3) from uric acid and dilute nitric acid (Ann. **147**, 367) ; (4) from convicin, a substance occurring in broad-beans, *Vicia faba minor*, and in vetches, *Vicia sativa*, when they are heated with sulphuric or hydrochloric acid (Ber. **29**, 2106).

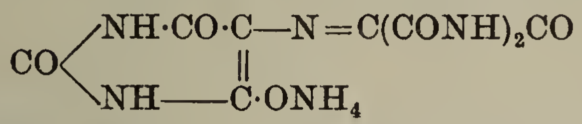
It crystallizes from hot H_2O in small, hard prisms with $3H_2O$ and turns red in an atmosphere containing ammonia. Its solution has an acid reaction ; ferric chloride and ammonia give it a deep-blue colour, and barium hydroxide solution produces a violet precipitate, which on boiling is converted into a mixture of barium alloxanate and dialurate. On boiling alloxantin with dilute sulphuric acid, it changes into the *ammonium* salt of *hydurilic acid*, $C_8H_6N_4O_6 + 2H_2O$. It combines with cyanamide, forming iso*uric acid*, $NC\cdot NHCH(CONH)_2CO$, which yields uric acid when boiled with hydrochloric acid, and *γ-thio*pseudo*uric acid*, $H_2N\cdot CS\cdot NHCH(CONH)_2CO$, when heated with ammonium sulphide (Ber. **38**, 2563).

Tetramethylalloxantin, *amalic acid*, $C_8(CH_3)_4N_4O_7$, is formed by the action of nitric acid or chlorine water on theine, or, better, by the reduction of dimethylalloxan (see above) with hydrogen sulphide (Ann. **215**, 258).

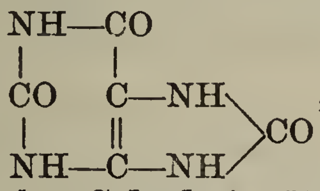
Purpuric acid, $C_8H_5N_6O_5$, is prepared from murexide (the salt of this acid) by passing hydrochloric acid gas into its solution in glacial acetic acid. It is an orange-red powder, which is immediately decomposed into alloxan and uramil by the action of water (J. pr. Chem. [2] 73, 463).

Murexide, $C_8H_4N_6O_5(NH_4) + H_2O$ (structural formula, see below), is the *ammonium salt* of *purpuric acid.* It is formed (1) from alloxantin and ammonium acetate and carbonate when they are heated ; (2) by mixing alloxan and uramil in ammoniacal solution ; (3) by careful oxidation of uric acid with dilute nitric acid (see above, Alloxantin) and adding ammonia to the residue on evaporation (*murexide reaction,* C. 1898, I. 665 : Ann. **333**, 28). It forms tables or prisms of a gold-green colour, which dissolve in water to a purple-red coloured solution. *Sodium purpurate,* $C_8H_4N_6O_5Na + H_2O$, is formed from murexide and sodium chloride ; *potassium purpurate* also from the di-potassium salt of uramil and iodine.

Hydrochloric acid decomposes murexide partially into uramil and alloxan, and partly into ammonia and alloxantin. 1 : 3-Dimethyluramil and alloxan, also 1 : 3-dimethylalloxan and uramil, give two different murexides, showing that the molecule is an unsymmetrical one. 5-Alkyluramils (p. 632) do not yield a murexide ; 7-alkyluramils lose alcohol and form salts of a simple purpuric acid ; therefore, purpuric acid is considered to be aci-*barbiturylimidoalloxan,* and murexide, the ammonium salt, to have the formula :



(Ann. **333**, 22 : C. 1904, II. 316 : J. pr. Chem. [2] **73**, 499).

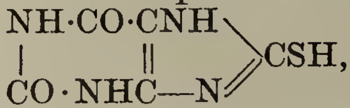
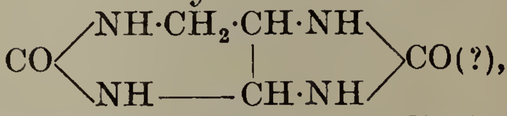
Uric acid, $C_5H_4N_4O_3$,  , is a white, crystalline, sandy powder, discovered by *Scheele* in 1776, in urinary calculi. It occurs in the fluids of the muscles, in the blood and in the urine, especially of the carnivoræ, whilst that of the herbivoræ contains mostly hippuric acid ; also, in the excrements of birds (guano), reptiles and insects. When urine is exposed for a while to the air, uric acid separates ; this also occurs in the organism (formation of gravel and joint concretions) in certain abnormal conditions.

History (Ber. **32**, 435).—*Liebig* and *Wöhler* (1826) showed that numerous derivatives could be obtained from uric acid. Their relationships and constitution were chiefly explained by *Baeyer* in 1863 and 1864. In consequence of certain experiments of *A. Strecker, Medicus* (1875) proposed the structural formula given above for the acid. This was conclusively proved by *E. Fischer* in his investigation of the methylated uric acids.

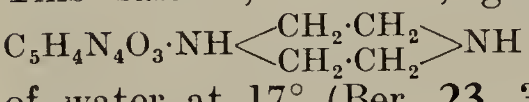
The results derived from analysis were confirmed by the synthesis made in 1888 by *R. Behrend* and *O. Roosen,* who proceeded from acetoacetic ester and urea (p. 639). *Horbaczewski* (1882–87) had previously made syntheses of uric acid at elevated temperatures, but obtained poor yields. They consisted in melting together glycocoll, trichlorolactamide, etc., with urea. No clue as to the constitution of the acid could be deduced from these. In 1895 *E. Fischer* and *Lorenz Ach* showed how *pseudo*uric acid (p. 639), previously synthesized by *A. Baeyer,* could, by fusion with oxalic acid, be converted into uric acid.

Preparation.—Uric acid is best prepared from guano or the excrements of reptiles.

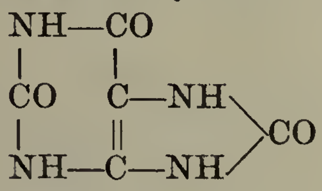
Properties.—Uric acid is a shining, white powder. It is odourless and tasteless, insoluble in alcohol and ether, and dissolves with difficulty in water ; 1 part requires 88,000 parts of water at 18° (C. 1900, II. 42) for its solution, and 1800 parts at 100°. (More recent solubility determinations, see Ann. **431**, 104.) Its solution remains long supersaturated. Its solubility is increased by the presence of salts like sodium phosphate and borate. Water precipitates it from its solution in concentrated sulphuric acid (Ber. **34**, 263). On evaporating uric acid to dryness with nitric acid, a yellow residue is obtained, which assumes a purple-red colour if moistened with ammonia, or violet with potassium or sodium hydroxides (*murexide reaction*, p. 635). When heated, uric acid decomposes into NH_3, CO_2, urea and cyanuric acid. The action of chloride and oxychloride of phosphorus on uric acid and alkyluric acids is of special importance in the chemistry of the uric acid group. The reaction is comparable to the conversion of acid amides into imidochlorides. The resulting compounds are highly reactive, whereby the chlorine can be exchanged for alkoxyl, hydroxyl, hydrosulphyl, the amino-group, iodine, and sometimes also hydrogen. The inter-connection between the members of the uric acid group can be elucidated by these chemical changes (Ber. **32**, 445).

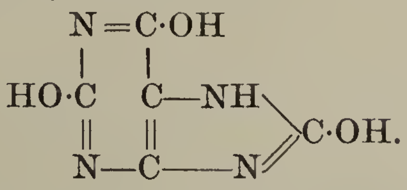
Carbon disulphide, when heated under pressure with uric acid, forms with it so-called *thioxanthine*,  $\left.\begin{array}{l}\mathrm{NH\cdot CO\cdot CNH}\\ \mathrm{|\qquad\quad \|}\\ \mathrm{CO\cdot NHC{-}N}\end{array}\right\rangle\mathrm{CSH}$, which also results when γ-thio*pseudo*uric acid (p. 634) is boiled with mineral acids (C. 1902, I. 548 : Ber. **34**, 2563). When heated with ammonium sulphide urea is converted into thiouramil (p. 633). Electrolytic reduction in sulphuric acid solution produces *purone*,  $\mathrm{CO}\left\langle\begin{array}{l}\mathrm{NH\cdot CH_2\cdot CH\cdot NH}\\ \mathrm{NH{-}{-}{-}CH\cdot NH}\end{array}\right\rangle\mathrm{CO(?)}$, a neutral body, together with the isomeric iso*purone*, soluble in alkalis and acids, which can also be produced by the transformation of purone, and *tetrahydrouric acid*, $C_5H_8N_4O_3$. Similar products are also obtained from the methylated uric acids (below) (Ber. **34**, 258). Formaldehyde unites with uric acid to form *mono-* and *di-formaldehyde addition products*, $C_5H_4N_4O_3 + CH_2O$ and $+ 2CH_2O$ (Ann. **299**, 340).

Salts.—Uric acid is a weak dibasic acid. (Acidity of the individual hydrogen atoms, see Ber. **53**, 2327 : **54**, 1676.) It forms monobasic hydrogen salts with the alkali carbonates. The normal alkali salts are obtained by dissolving the acid in potassium or sodium hydroxide. When CO_2 is conducted through the alkaline solution, the primary salts are precipitated.

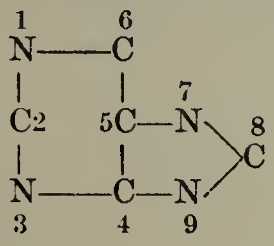
The *potassium salt*, $C_5H_3N_4O_3K$, dissolves in 800 parts of water at 20° ; the *sodium* and *ammonium salts* are more insoluble ; *lithium salt* (Lipowitz) is much more soluble (in 368 parts of water at 19°) (Ann. **122**, 241), hence lithium mineral waters are used in such diseases where there is an abnormal metabolism of uric acid. This salt is, however, greatly surpassed by the *piperazine salt*,  $\mathrm{C_5H_4N_4O_3\cdot NH}\left\langle\begin{array}{l}\mathrm{CH_2\cdot CH_2}\\ \mathrm{CH_2\cdot CH_2}\end{array}\right\rangle\mathrm{NH}$ (Finzelberg), which dissolves in 50 parts of water at 17° (Ber. **23**, 3718). The *lysidine* or *methylglyoxalidine salt* (Ladenburg) is even more soluble (1 part in 6 parts of water ; Ber. **27**, 2952). In actual practice, these compounds are not of much value in the treatment of gout.

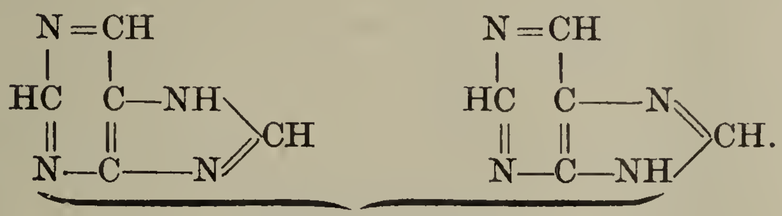
Methyluric acids (Ber. **32**, 2721 ; Ann. **309**, 260).—The four hydrogen atoms in uric acid can be replaced by methyl groups. In all methyluric acids, including tetramethyluric acid, the methyl groups are linked to nitrogen ; this, in conjunction with the decompositions and synthesis of uric acid, argues for formula I, without, however, in the light of our present representations, excluding formulæ such as II (*cf.* below, the isomeric 3-methyluric acids):

I. 

II. 

To indicate the position of the methyl groups in the methyluric acids and the constitution of other bodies containing the same hetero-twin ring, E. Fischer suggested that the carbon and nitrogen atoms of the nucleus contained in uric acid and bodies related to it be numbered, and that the hydrogen compound of the nucleus, C_5N_4, which could have two formulæ, should be called "*purine*" (from *purum* and *uricum*).

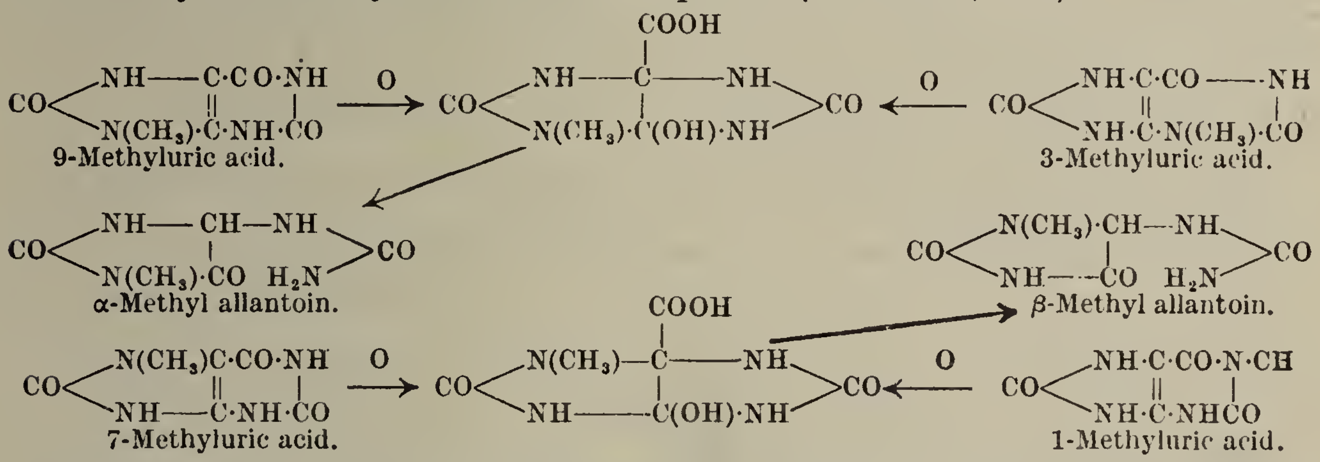




Purine (Ber. **32**, 449).

The methyluric acids are obtained (1) by treatment of lead and potassium urates and methylurates with iodomethane; (2) from the formaldehyde uric acid compound (p. 636) by reduction (C. 1900, II. 459); (3) from the corresponding *pseudo*uric acid (p. 632) through loss of water. Whilst formula I for uric acid indicates the possibility of only four isomeric monomethyluric acids, actually six are known, as well as six dimethyluric acids, four trimethyluric acids and one tetramethyluric acid.

9-*Methyluric acid* is obtained together with 3-*methyluric acid* from uric acid (Ann. **413**, 98: Ber. **52**, 768, 784): the former yields, by the action of nitric acid, alloxan. 3-Methyluric acid is best obtained synthetically by Traube's method (Ber. **53**, 769) and yields on oxidation with nitric acid methylalloxan. 7-*Methyluric acid* is obtained from 7-methyl*pseudo*uric acid. 1-*Methyluric acid* is formed from monomethylalloxan (Ber. **32**, 2721). 3-Methyluric acid yields on permanganate oxidation the same α-methylallantoin as is formed from 9-methyluric acid, and similarly 1- and 7-methyluric acids yield the same β-methylallantoin; this can be explained by the assumption of the intermediate formation of a common symmetrically constituted compound (Ann. **333**, 145).



3 : 9-*Dimethyluric acid* (α) is obtained from basic lead urate and iodomethane. 7 : 9-*Dimethyluric acid* (β) (Ber. **17**, 1780). 1 : 3-*Dimethyluric acid* (γ) is prepared from 1 : 3-dimethyl*pseudo*uric acid (p. 632); and from 1 : 3-dimethyl-4 : 5-diaminouracil (see also Theophylline, p. 644). 3 : 7-*Dimethyluric acid* (δ) is formed from 7-methyluric acid (see also Theobromine, p. 643). 1 : 7-*Dimethyluric acid* is produced from 1 : 7-dimethyl*pseudo*uric acid: 1 : 9-*dimethyluric acid* (Ber. **32**, 464).

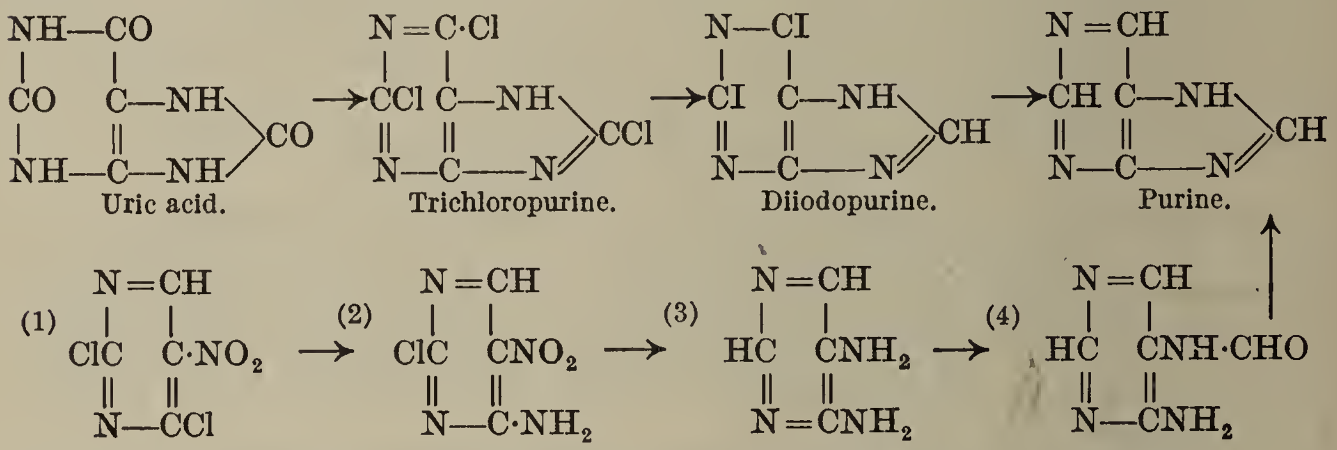
1 : 3 : 7-*Trimethyluric acid*, prepared from 1 : 3 : 7-trimethyl*pseudo*uric acid (α), is identical with hydroxycaffeine (Ber. **30**, 567). 3 : 7 : 9-*Trimethyluric acid* (α) is formed from 7 : 9-dimethyluric acid. 1 : 3 : 9-*Trimethyluric acid* is produced from 1 : 3-dimethyluric acid. 1 : 7 : 9-*Trimethyluric acid* (Ber. **32**, 466).

Tetramethyluric acid is prepared from potassium trimethyl urate and iodomethane. Isomeric with it is *methoxycaffeine,* 1 : 3 : 7-trimethyl-2 : 6-dioxy-8-methoxypurine, which is prepared from bromo- or chloro-caffeine by the action of sodium hydroxide in methyl alcohol (Ber. **32**, 467).

Phenyluric acid is prepared from phenyl*pseudo*uric acid (p. 633) (C. 1900, I. 806).

Purine, $C_5N_4H_4$, m.p. 216°, is the fundamental compound of the uric acid group (p. 637). It cannot be obtained directly from uric acid, but it is prepared by converting uric acid by $POCl_3$ (p. 641) into *trichloropurine,* which, with hydriodic acid at 0°, gives 2 : 6-*diodopurine* ; this, on reduction with zinc dust and water, results in purine.

Purine, like uric acid, can also be synthesized as follows :—synthetic methyluracil is converted into 5-nitrouracil (p. 639) ; this, with $POCl_3$, yields 2 : 4-dichloro-5-nitropyrimidine (1), which with ammonia gives 2-chloro-4-amino-5-nitropyrimidine (2) ; reduction with hydriodic acid gives 4 : 5-diaminopyrimidine (3), of which the formyl-derivative (4), obtained by the action of formic acid, is decomposed when heated with water, when purine is formed :



Purine reacts simultaneously as an acid and as a strong base. It is easily soluble in water, and is stable towards oxidizing agents.

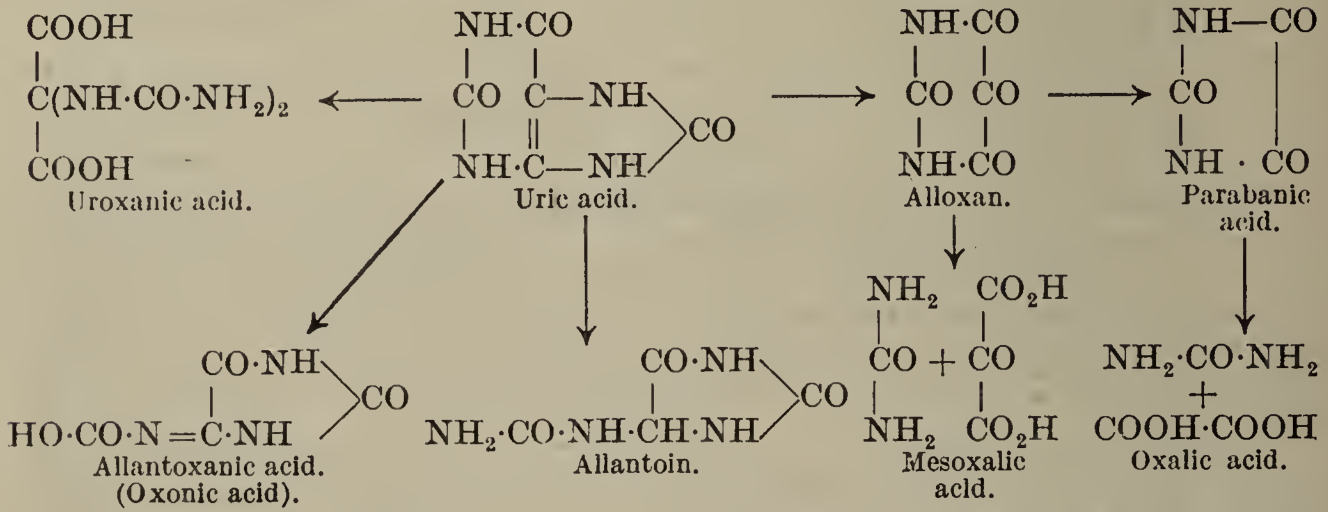
Methylpurines and other simple purine derivatives are obtained similarly (Ber. **31**, 2550 : **39**, 250).

Oxidation of Uric Acid

When uric acid is oxidized with ordinary nitric acid the products are alloxan (mesoxalylurea) and parabanic acid (oxalylurea) : this oxidation proceeds through the stage of the 4 : 5-uric acid glycol (Biltz, Ber. **43**, 1511). By the action of permanganate or a solution of iodine in alkali (Ber. **27**, R. 902), allantoin, together with uroxanic acid, $C_5H_8N_4O_6$, is produced : *uroxanic acid,* decomp. 162°, is diureidomalonic acid, $(NH_2 \cdot CO \cdot NH)_2C(COOH)_2$, and changes into allantoin on prolonged standing in contact with hydrochloric acid (Ber. **53**, 1950 : formation from uric acid, Ber. **53**, 1964).

Allantoxanic acid (oxonic acid) is also obtained by the oxidation of uric acid by alkaline permanganate (Ber. **53**, 1971).

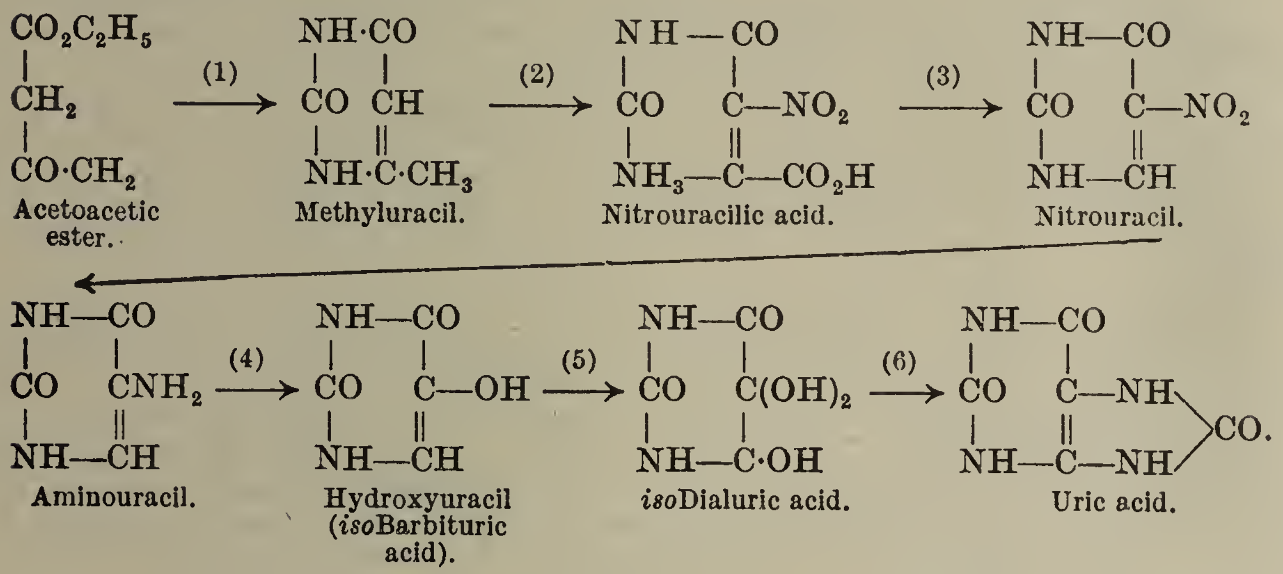
These decompositions are represented in the following scheme :—



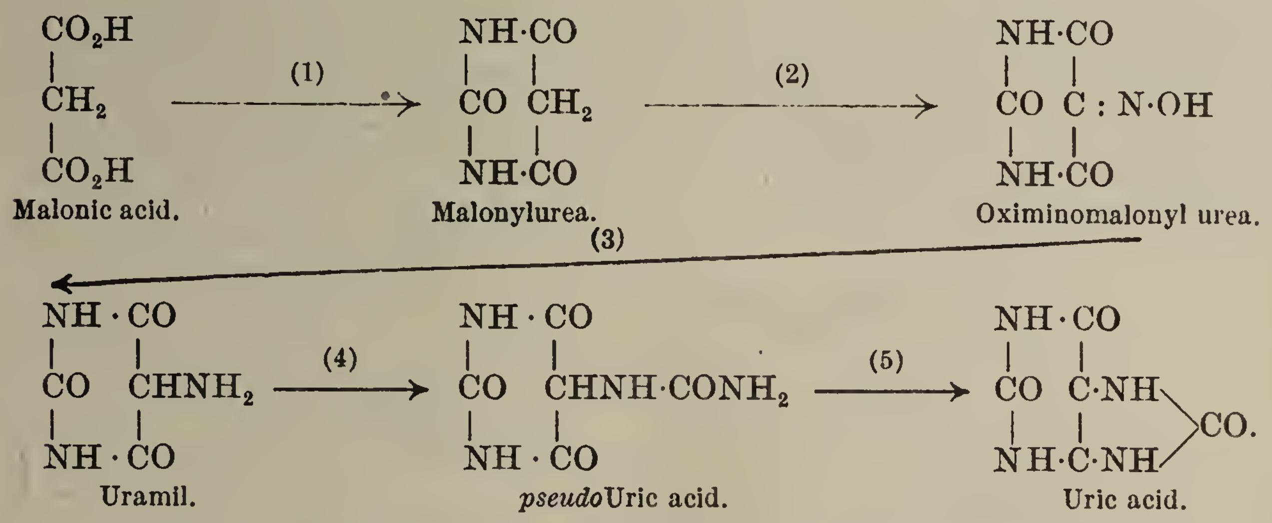
Uric acid is the diureide of the hypothetical body, $C(OH)_2{=}C(OH)—CO_2H$, the *pseudo*-form of the semi-aldehyde of mesoxalic acid, $CHO \cdot CO \cdot CO_2H$ (p. 600).

Synthesis of Uric Acid : (1) *from Acetoacetic Ester :* (2) *from Malonic Acid :* (3) *Cyanoacetyl Urea*

(1) From **acetoacetic ester :** (1) Acetoacetic ester and urea unite to β-uramidocrotonic ester. When this is hydrolysed with alkali it yields an acid which, in a free state, splits off water and becomes a cyclic ureide—*methyluracil.* (2) Nitric acid converts the latter into *nitrouracil carboxylic acid,* (3) whose potassium salt when boiled with water loses a molecule of carbon dioxide, and becomes converted into the potassium salt of *nitrouracil.* (4) The reduction of the latter with tin and hydrochloric acid gives in part *aminouracil* (Ann. **309,** 256) and in part hydroxyuracil or iso*barbituric acid.* (5) Bromine water oxidizes the latter to iso*dialuric acid,* which when heated (6) with urea and sulphuric acid yields *uric acid* (Ann. **251,** 235).



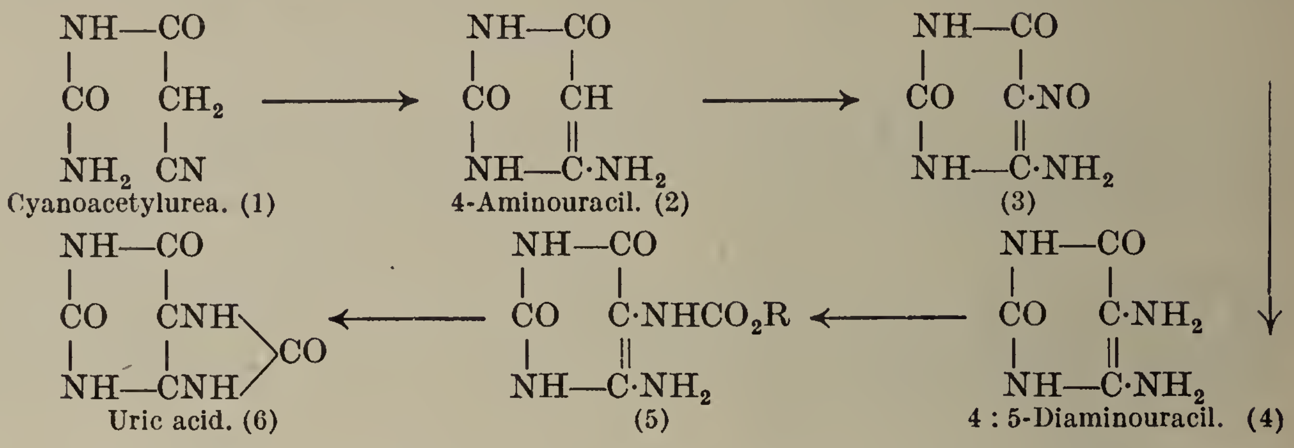
(2) From **malonic acid :** (1) Urea and malonic acid yield *malonylurea,* which (2) nitrous acid converts into oximinomalonylurea or *violuric acid.* (3) When the latter is reduced, aminomalonylurea or *uramil* results. (4) This is changed by potassium cyanate into *pseudo*uric acid. (5) On withdrawing water from *pseudo*uric acid by means of molten oxalic acid or boiling hydrochloric acid, *uric acid* results (Ber. **30,** 559) :



Since alloxan and dimethylalloxan yield methylated *pseudo*uric acids, methylated uric acids can also be synthesized in this way.

(3) From **Cyanoacetyl urea :** Urea and cyanoacetic acid are condensed to (1) *cyanoacetylurea,* and this to (2) 4-*aminouracil* or 4-amino-2 : 6-dioxypyrimidine (C. 1906, II. 1590 : Ber. **41,** 532). This, with nitrous acid, gives (3) a *nitroso*-compound which, with ammonium sulphide, is reduced to (4) 4 : 5-*diaminouracil.* The diamine reacts with chlorocarbonic ester and aqueous sodium hydroxide to form (5) a *urethane,* the sodium compound of which when heated

to 180–190° is converted into (6) *sodium urate* (W. Traube, Ber. **33**, 3035: Ann. **331**, 64):


Cyanoacetylurea. (1) 4-Aminouracil. (2) (3) 4 : 5-Diaminouracil. (4) (5) Uric acid. (6)

This synthesis can be employed generally with the following modifications:—

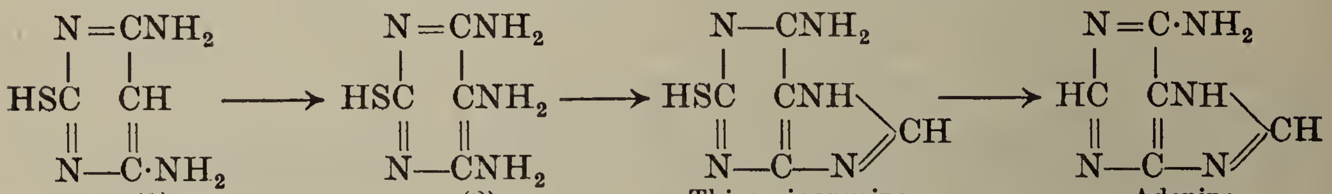
(1) Replacement of the urea by methylated ureas in the condensation with cyanoacetic acid to obtain *methylated uric acids*.

(2) Replacement of the chlorocarbonic ester by formic acid; formyl diaminouracil is formed, the sodium compound of which, on being heated, yield *xanthine* or *methylated xanthines* (pp. 642–3).

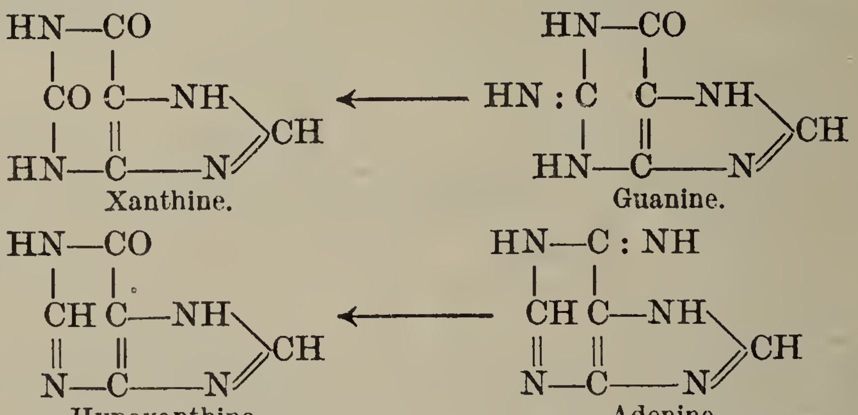
(3) Condensation of guanidine, instead of urea, with cyanoacetic acid to form 2 : 4-diamino-6-oxypyrimidine; this is ultimately transformed into *guanine* (p. 642).

(4) Condensation of cyanoacetic acid with thiourea to form 2-thio-4-amino-6-oxypyrimidine. This is converted into thio-oxypurine which, when oxidized by nitric acid, yields sulphuric acid and *hypoxanthine* (p. 642).

(5) Condensation of malonic nitrile with thiourea to form 2-thio-4 : 6-diaminopyrimidine (below), which, analogously to the above, is converted through its nitroso-compound into 2-thio-4 : 5 : 6-triaminopyrimidine (2), of which the potassium salt of the formyl-compound, when heated, yields 2-thio-6-aminopurine (3); oxidation with H_2O_2 produces sulphuric acid and *adenine* (4):


(1) (2) Thioaminopurine. (3) Adenine. (4)

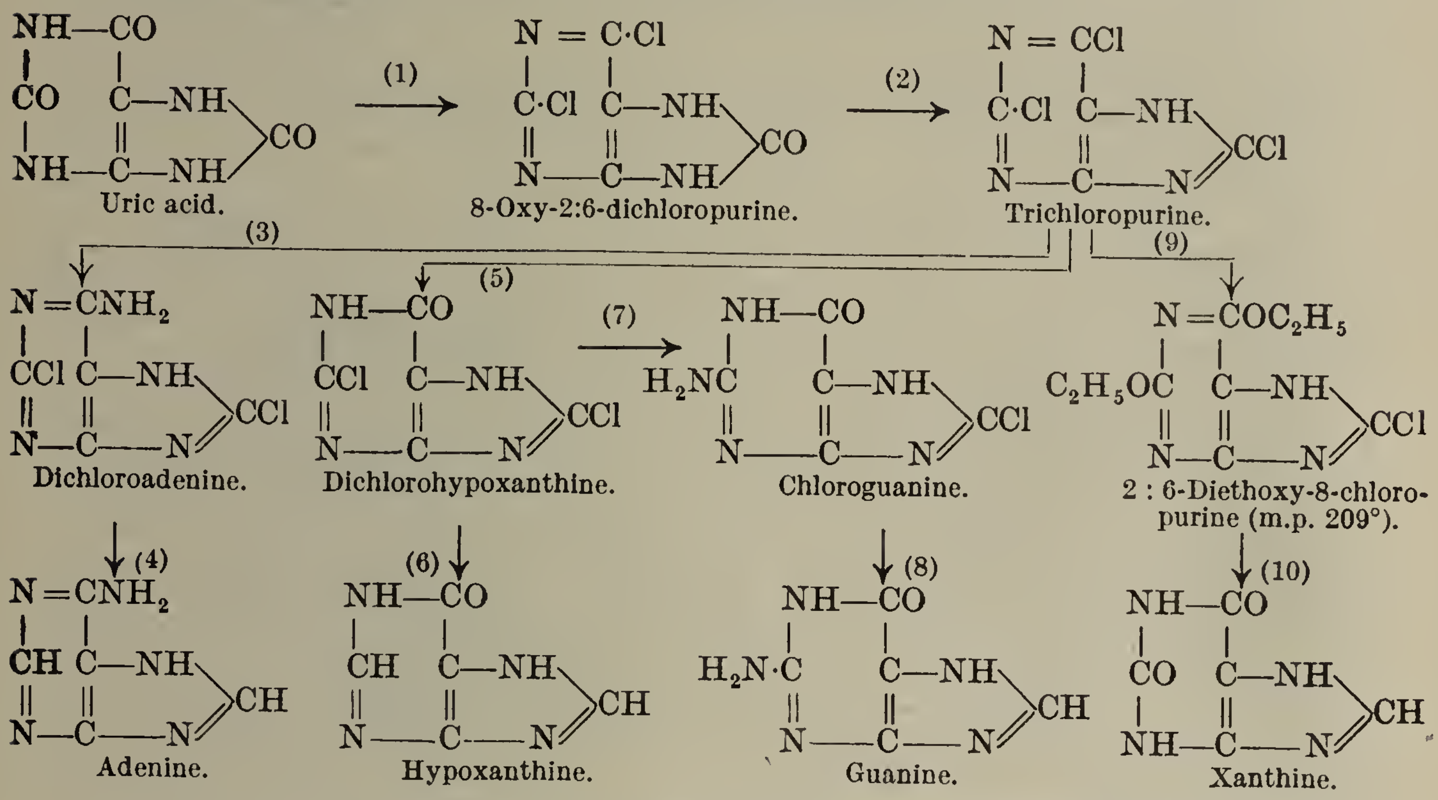
Xanthine Group.—Guanine, xanthine, hypoxanthine, and adenine stand in close relation to uric acid. Like it, they occur as products of the metabolism of the animal organism, and are most easily produced from *nucleic acids* (p. 748) by boiling them with water (*cf.* Ber. **37**, 708). Xanthine and hypoxanthine occur in the extract of tea. Bodies of the xanthine group are found in the juice of the sugar beet (Ber. **29**, 2645).


Xanthine. Guanine. Hypoxanthine. Adenine.

Guanine is changed into xanthine by the action of nitrous acid and yields guanidine on decomposition (p. 512). It is, therefore, to be regarded as being xanthine in which a guanidine residue takes the place of a urea residue, *i.e.* the oxygen of a CO-group is replaced by NH. *Adenine* stands in similar relation to hypoxanthine as guanine to xanthine, in that its conversion into hypoxanthine is brought about by nitrous acid.

Conversion of Uric Acid into Xanthine, Guanine, Hypoxanthine and Adenine

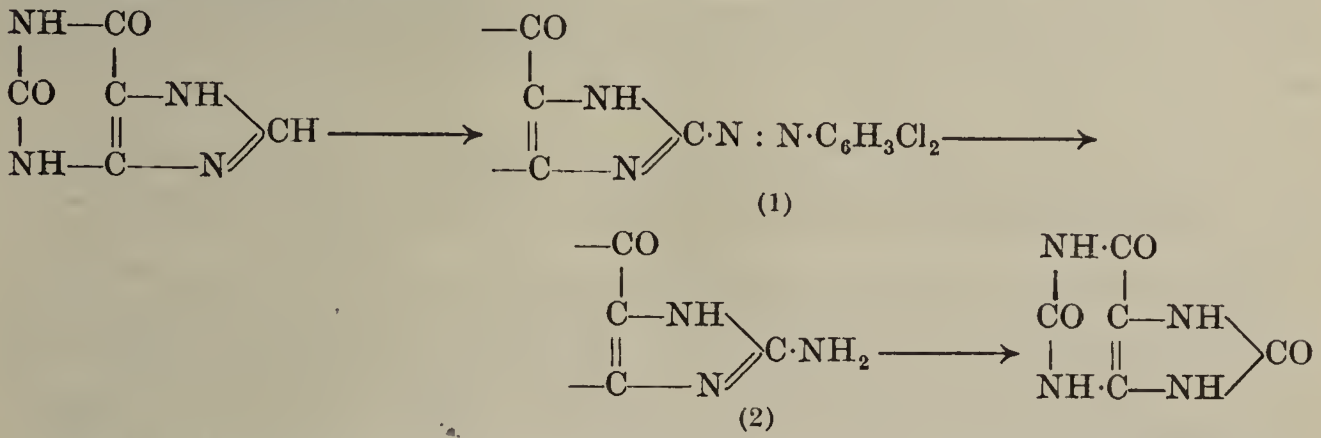
Potassium urate and phosphorus oxychloride produce 8-oxy-2 : 6-dichloropurine, which on further treatment with phosphorus oxychloride yields 2 : 6 : 8-trichloropurine, m.p. 188°. The latter is a weak acid, and gives, on methylation, a mixture of the two isomeric forms of methyltrichloropurine.



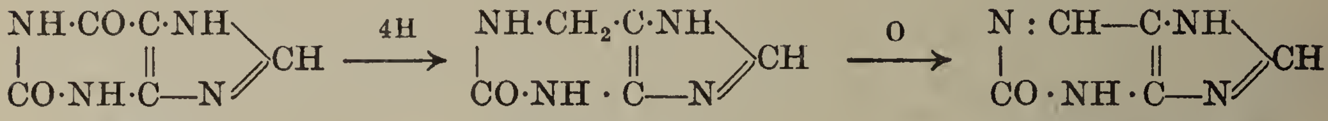
The chlorine atoms 2 and 6 are easily substituted in the presence of alkalis by OH, C_2H_5O, and NH_2; but in the 8-position the chlorine atom can be replaced by hydroxyl, by fuming hydrochloric acid, but not by alkalis. On this behaviour is based the synthesis of xanthine, guanine, hypoxanthine and adenine (Ber. **30**, 2220, 2226).

Uric acid is (1) acted on by $POCl_3$ to form 8-*oxy*-2 : 6-*dichloropurine*, and is similarly (2) converted into *trichloropurine*. The latter, with aqueous ammonia at 100° gives (3) *dichloroadenine*, with aqueous KOH at 100° (5) *dichlorohypoxanthine*, and with sodium ethoxide (9), 2 : 6-*diethyoxy*-8-*chloropurine*. These three substances, when reduced with hydriodic acid, yield (4) *adenine*, (6) *hypoxanthine*, and (10) *xanthine*. Further, dichlorohypoxanthine and alcoholic ammonia (7) yield *chloroguanine*, and this, with hydriodic acid, (8) *guanine*.

The reverse change, from xanthine to uric acid, can be brought about by coupling the xanthine with dichlorobenzenediazonium chloride to yield the azo-compound (1), which can be reduced with sodium hydrosulphite to the amino-compound (2) and the latter converted into uric acid by nitrous acid (*H. Fischer*, Z. physiol. Chem. **60**, 69).



Xanthine and the methylated xanthines (p. 643) are reduced electrolytically in sulphuric acid solution, whereby the oxygen atom in position 6 is replaced by two hydrogen atoms to form the *desoxy*-compound, which easily loses two hydrogen atoms by oxidation to form *oxypurine*. Similarly, guanine yields *desoxyguanine* and this 2-*aminopurine* ; similarly with adenine (*Tafel*, Ber. **33**, 3369 : **34**, 1165) :

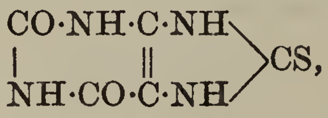


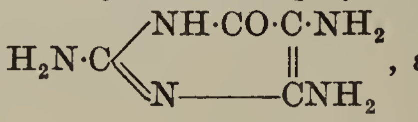
Xanthine. Desoxyxanthine. 2-Oxypurine (isomeric with hypoxanthine).

Desoxyxanthine, *desoxyheteroxanthine*, and *desoxyparaxanthine* are decomposed by acids into CO_2, NH_3 and iminazolone derivatives :

whilst *desoxytheophylline* and *desoxycaffeine*, xanthines, in which the methyl group occupies the 3-position, are far more stable (Ber. **41**, 2546).

Xanthine, 2 : 6-*dioxypurine*, $C_5N_4H_4O_2$ (constitutional formula, above), occurs in small quantities in animal secretions, such as urine, blood, the liver, and sometimes in urinary calculi ; it is found, also, in extract of tea. It is prepared by the action of nitrous acid on guanine in sulphuric acid solution (Ber. **32**, 468) ; also, by heating the sodium salt of formyl-4 : 5-diaminouracil (p. 640) to 220°. It forms a white amorphous mass, which is somewhat soluble in boiling water, and combines with both acids and alkalis. It dissolves easily in boiling ammonia, from a solution in which silver nitrate precipitates a compound, $C_5H_2Ag_2N_4O_2 + H_2O$. The corresponding lead compound is converted into theobromine (dimethylxanthine) when heated with iodomethane at 100°. Methylation in alkaline aqueous solutions produces caffeine. When heated with potassium chlorate and hydrochloric acid, xanthine (analogously to caffeine, p. 644) is broken down into alloxan and urea.

8-*Thioxanthine*,  is formed when γ-thio*pseudo*uric acid (p. 634) is heated ; and from 4 : 5-diaminouracil (p. 640), and carbon disulphide (C. 1903, II. 80).

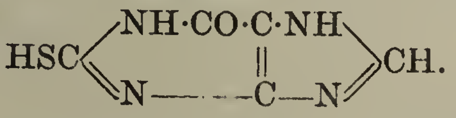
Guanine, 2-*amino*-6-*oxypurine*, $C_5N_5H_5O$ (constitutional formula, p. 641), occurs in the pancreas of some animals, and particularly in guano ; also in the silvery matter of the scales of bleak, *Alburnus lucidus* (C. 1898, I. 1132). It is readily synthesized by converting cyanoacetylguanidine (p. 640) into triaminooxypyrimidine,  , and heating this with formic acid (Ber. **33**, 1371).

Guanine forms an amorphous powder, insoluble in water, alcohol and ether. It combines with one and two equivalents of acids forming crystalline salts, such as $C_5H_5N_5O \cdot 2HCl$; and also with alkalis to form crystalline compounds. Silver nitrate precipitates a crystalline compound, $C_5H_5N_5O \cdot AgNO_3$, from a nitric acid solution of the substance. Nitrous acid converts guanine into xanthine. Potassium chloride and hydrochloric acid decompose it into parabanic acid, guanidine and carbon dioxide (p. 512).

Bromoguanine is formed from guanine and bromine. Fuming hydrochloric acid converts it into 2-amino-6:8-dioxypurine. *Chloroguanine* is prepared from dichlorohypoxanthine and alcoholic ammonia. With hydriodic acid it yields guanine.

Hypoxanthine, 6-*oxypurine*, $C_5N_4H_4O$ (constitutional formula, p. 641), almost invariably accompanies xanthine in the animal organism, and can be differentiated from it particularly by the slight solubility of its hydrochloride. It forms needles, soluble with difficulty in water, but soluble in acids and alkalis, and in ammoniacal solution is precipitated by silver nitrate which forms $C_5H_2Ag_2N_4O + H_2O$.

Dimethylhypoxanthine is decomposed when heated with hydrochloric acid into methylamine and sarcosine (p. 441) (Ber. **26**, 1914). The position of the oxygen atom is determined by the transformation of adenine into hypoxanthine by nitrous acid ; also by its formation from the decomposition of the synthetic 2-thio-6-oxypurine



$$HSC\begin{matrix} \diagup NH\cdot CO\cdot C\cdot NH \diagdown \\ \qquad\qquad\quad \Vert \\ \diagdown\!\!\diagdown N\text{———}C\text{—}N \diagup\!\!\diagup \end{matrix}CH.$$

Adenine, 6-*aminopurine*, $C_5N_5H_5$ (constitutional formula, p. 641), m.p. 360–368° (decomp.) (Ber. **30**, 2242), is a polymer of hydrocyanic acid. It is obtained from the pancreas of cattle, and occurs in extract of tea. It crystallizes with 3 molecules of water in mother-of-pearl crystals, which lose water at 54° and turn white. Nitrous acid converts it into hypoxanthine ; hydrochloric acid at 180–220° into glycocoll, ammonia, formic acid and carbon dioxide (*Kossel*, Ber. **23**, 225 : **26**, 1914). The position of the amino-group is fixed by the connection of adenine with 6-amino-2:8-dioxypurine through dichloroadenine ; fuming hydrochloric acid converts dichloroadenine into 6-amino-2:8-dioxypurine, which on decomposition does not yield guanidine, showing that the amino-group must be in the 6-position and not in the 2 or 8.

Synthesis of adenine from 2-thio-4 : 5 : 6-triaminopyrimidine (p. 640). The analogous formation of purine derivatives still richer in nitrogen, such as 2-*amino-adenine*, $C_5N_4H_2(NH_2)_2$, from malonic nitrile, guanidine, etc., see Ber. **37**, 4544.

Methylxanthines.—Heteroxanthine, theobromine, paraxanthine, theophylline, theine (or caffeine), are all methyl derivatives of xanthine.

Heteroxanthine, 7-*methylxanthine*, $C_5H_3N_4O(CH_3)$, occurs in small quantities in urine, and is formed from theobromine by the loss of methyl. By methylation it is converted into caffeine ; hydrochloric acid decompose it into sarcosine (Ber. **32**, 469). Electrolytic reduction produces *desoxyheteroxanthine*, which on oxidation forms 7-*methyl*-2-*oxypurine* (*cf.* p. 642). The isomeric 3-*methylxanthine* is prepared from 3-methyluric acid (p. 637), and also from cyanoacetylmethylurea, $CN\cdot CH_2CO\cdot NHCONH\cdot CH_3$, as shown in diagram 3 of the uric acid synthesis (p. 640).

Theobromine, 3 : 7-*dimethylxanthine*, $C_5H_2N_4O_2(CH_3)_2$, occurs in the cocoa beans of *Theobroma cacao* ; it is artificially prepared by methylating xanthine (p. 642) or 3-methylxanthine (Ber. **33**, 3050).

Theobromine forms a bitter-tasting crystalline powder, slightly soluble in hot water and alcohol, but is fairly easily soluble in ammonia. It sublimes unchanged when carefully heated at 290°. Its reaction is neutral, but it forms crystalline salts with acids, which are decomposed by excess of water. Its silver salt, $C_7H_7AgN_4O_2$, and iodomethane produce caffeine. Electrolytic reduction produces *desoxytheobromine*, which on oxidation yields 3 : 7-*dimethyl*-2-*oxypurine* (*cf.* p. 642). Theobromine on oxidation is converted into oxy-3 : 7-dimethyluric acid (Ber. **31**, 1450) ; potassium chlorate and hydrochloric acid decompose it into monomethylalloxan and monomethylurea. The action of dry chlorine on theobromine (Ber. **30**, 2604).

pseudo*Theobromine* is formed from the silver xanthine compound and iodomethane (C. 1898, I. 1132).

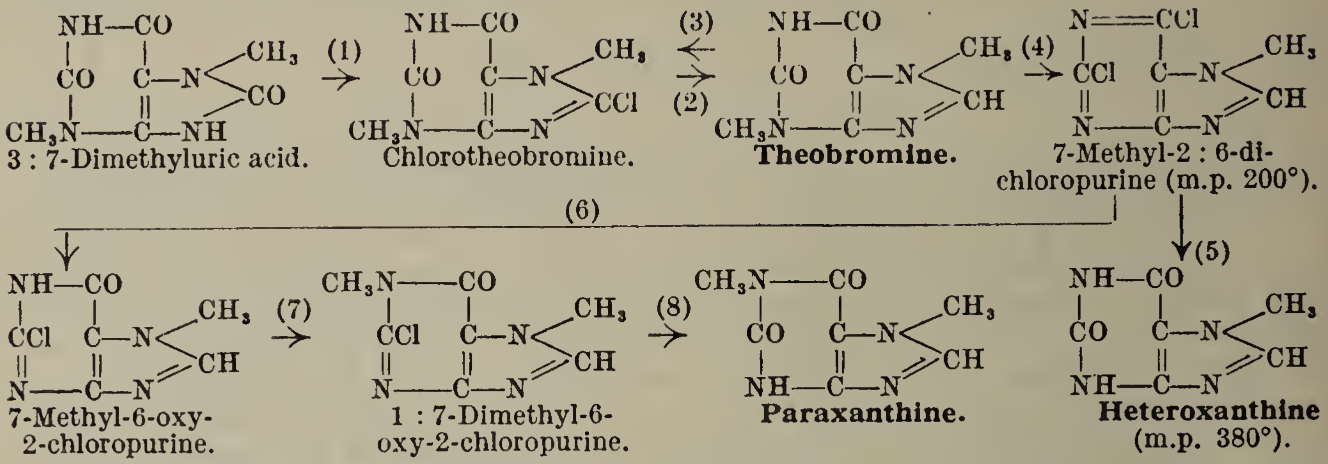
Paraxanthine, 1:7-*dimethylxanthine*, $C_5H_2N_4O_2(CH_3)_2$, m.p. 289°, occurs in urine (Ber. **18**, 3406). It is prepared from theobromine by the removal of methyl and its replacement in another position (see below for synthesis). It is obtained from 1 : 7-dimethyluric acid, as theobromine is from the 3 : 7-compound (Ber. **32**, 471). Methylation produces caffeine (Ber. **30**, 554).

Synthesis of Heteroxanthine, Theobromine, and Paraxanthine

7-Methyl*pseudo*uric acid yields 7-methyluric acid, which by methylation gives 3 : 7-dimethyluric acid. $POCl_3$ converts (1) 3 : 7-*dimethyluric acid* into chlorotheobromine, which is reduced (2) by hydriodic acid to theobromine, and which is formed from theobromine (3) by iodine chloride.

When theobromine is heated with $POCl_3$ and PCl_5 (4) it loses a methyl group and forms 2 : 6-dichloro-7-methylpurine which with hot fuming hydrochloric acid (5) gives heteroxanthine. If 2 : 6-dichloro-7-methyl purine is boiled with dilute aqueous sodium hydroxide, it is converted into 6-oxy-2-chloro-7-methylpurine. If the potassium salt of this body is methylated (7), there is formed 6-oxy-

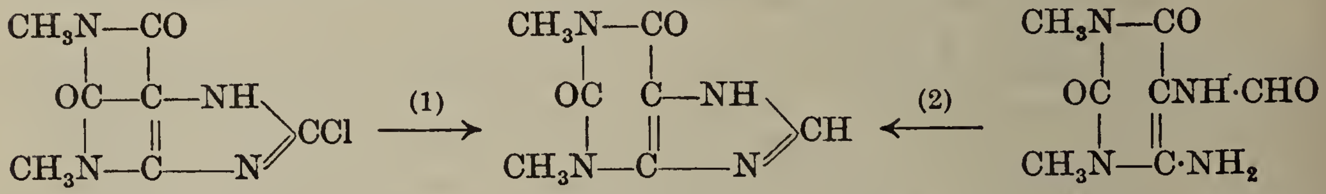
2-chloro-1 : 7-dimethylpurine from which hot fuming hydrochloric acid produces (8) paraxanthine (Ber. **32**, 469).



The constitution of 6-oxy-2-chloro-7-methylpurine is so assigned, because its reaction product with ammonia gives guanidine when oxidized with chlorine, so that it must be 6-oxy-2-amino-7-methylpurine. This establishes the constitution of heteroxanthine.

The product of methylating 6-oxy-2-chloro-7-methylpurine can only have the second methyl group in the 1-position, whereby the 1:7-position of the methyl group in paraxanthine is determined.

Theophylline, 1 : 3-*dimethylxanthine,* m.p. 264°, was discovered in 1888 by *Kossel* in tea extract. By the action of methyl iodide on silver theophylline he obtained caffeine (Ber. **21**, 2164). Theophylline has been synthetically prepared from 1 : 3-dimethyluric acid by its conversion with PCl_5 into *chlorotheophylline,* m.p. 300° (decomp.); hydriodic acid reduces this to theophylline (*E. Fischer,* Ber. **30**, 553). A shorter synthesis is from cyanoacetyldimethylurea, $CN{\cdot}CH_2{\cdot}CON(CH_3)CONH{\cdot}CH_3$, in which, following diagram 3 of the uric acid synthesis (p. 640), this body is converted into: 1 : 3-dimethyl-4 : 5-diaminouracil, of which the formyl-compound (2) is converted into theophylline when warmed with alkalis (Ber. **33**, 3052 : C. 1903, I. 370).



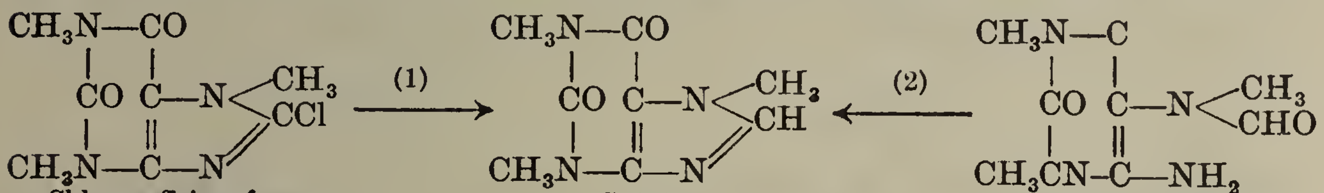
Caffeine, *theine,* 1 : 3 : 7-*trimethylxanthine,* $C_8H_{10}N_4O_2$, m.p. 239°, occurs in the leaves and beans of the coffee tree (0·5 per cent.), in tea (2–4 per cent.), in Paraguay tea (from *Ilex paraguayensis*), in guarana (about 5 per cent.), the roasted pulp of the fruit of *Paullinia sorbilis,* and in kola nuts (3 per cent.). It is also found in minute quantities in cocoa. It is used in medicine as a nerve stimulant and diuretic.

Caffeine crystallizes with one molecule of water. It has a feeble bitter taste, and forms salts with the strong mineral acids, which are readily decomposed by water. On evaporating a solution of chlorine water containing traces of caffeine there remains a reddish-brown spot, which acquires a beautiful violet-red colour when dissolved in ammonia. Sarcosine, $NHMe{\cdot}CH_2{\cdot}COOH$, is obtained by warming caffeine with baryta water. On electrolytic reduction, desoxycaffeine (p. 642) is produced.

By the action of sodium hydroxide, caffeidinecarboxylic acid, $C_7H_{11}N_4O{\cdot}COOH$, is produced, which readily breaks down into caffeidine, $C_7H_{12}N_4O$, and carbon dioxide (Ber. **16**, 2309). Further derivatives of caffeine, apocaffeine, caffuric acid and caffoline (1 : 3 : 6-trimethylallantoin) are discussed in Ber. **44**, 282.

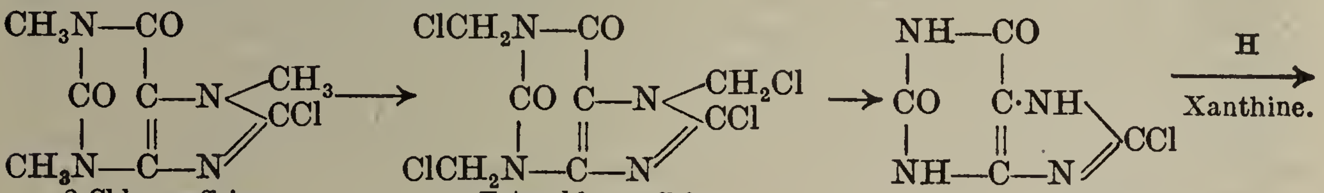
Chlorine water breaks caffeine up into dimethylalloxan and methylurea (p. 633). Chlorine and bromine convert caffeine into *chlorocaffeine,* m.p. 180°, and *bromocaffeine,* m.p. 206°. Zinc dust reduces both of them to caffeine; ammonia and bromocaffeine produce *aminocaffeine,* which behaves like an aromatic amine (Vol. II) in so far that it yields *diazocaffeine* with nitrous acid, which can be coupled to form *caffeine diazo-* bodies (C. 1900, I. 407). Sodium methoxide converts chlorocaffeine into *methoxycaffeine,* m.p. 174°, which when heated to 200° is converted into tetramethyluric acid (Ber. **35**, 1991). The latter is decomposed by hydrochloric acid into chloromethane and *hydroxycaffeine*, m.p. 345°. This is identical with 1 : 3 : 7-trimethyluric acid. PCl_5 converts hydroxycaffeine into chlorocaffeine. Proceeding from dimethylalloxan, 1 : 3 : 7-trimethyluric acid may be synthetically made (p. 637), and from this caffeine through chloro-caffeine. Furthermore, the lower homologues of caffeine—theobromine and theophylline—can be synthesized, and by introducing methyl into them caffeine will result. This, then, is an additional synthesis of caffeine (*E. Fischer*, Ber. **30**, 549).

Finally, caffeine can be produced from the already synthesized 1 : 3-dimethyl-4 : 5-diaminouracil (see above, theophylline) by preparing the formyl-compound, methylating it (below) and heating the product (Ber. **33**, 3054) :



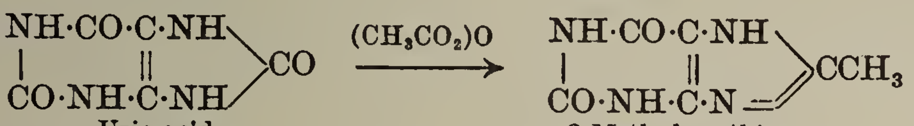
Chlorocaffeine, from 1 : 3 : 7-Trimethyluric acid. Caffeine. Formyl-4 : 5-diamino-1 : 3 : 7-trimethyluracil.

Just as caffeine can be built up by exhaustive methylation of xanthine and the lower methylxanthines, so these bodies are obtained by the breaking down of caffeine. Chlorocaffeine (see above) treated with chlorine and $POCl_3$ at low temperatures gives a product in which the 7-methyl group is chlorinated, whilst at higher temperatures the 3-methyl group is attacked ; if excess of chlorine be employed a tetrachlorocaffeine results, in which all three methyl groups are chlorinated. When boiled with water, these methyl groups are lost in the form of formaldehyde, and by reduction hydrogen may be exchanged for the chlorine in the 8-position (Ber. **39**, 423) :



8-Chlorocaffeine. Tetrachlorocaffeine. 8-Chloroxanthine.

8-*Alkylxanthines* are obtained from the corresponding uric acids by heating them with carboxylic anhydrides (C. 1901, II. 71).



Uric acid. 8-Methylxanthine.

The methyl group in these substances is easily chlorinated : 8-trichloromethylxanthines are obtained and can be converted into xanthine-8-carboxylic acids, such as 3-*methylxanthine*-8-*carboxylic acid*, $C_5H_2N_4O_2(CH_3)CO_2H$, *caffeine*-8-*carboxylic acid*, $C_5H_4O_2(CH_3)_3CO_2H$, *theobromine*-8-*carboxylic acid*, $C_5HN_4O_2(CH_3)_2CO_2H$. The acids lose CO_2 when boiled with water (C. 1904, II. 625).

Carnine, $C_7H_8N_4O + H_2O$, has been found in meat extracts. It is a powder, fairly soluble in hot water, which forms a crystalline compound with hydrochloric acid. Bromine water or nitric acid produces sarcine.

18. TRICARBOXYLIC ACIDS

A. SATURATED TRICARBOXYLIC ACIDS

(*a*) Tricarboxylic Acids with Two or Three Carboxyl Groups attached to the Same Carbon Atom

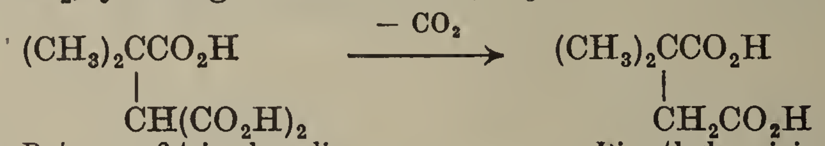
Formation.—(1) By the action on the sodium compounds of malonic esters, $CHNa(CO_2R')_2$, and alkylmalonic esters, $R{\cdot}CNa(CO_2R')_2$—of halogen fatty esters such as chlorocarbonic ester, chloroacetic ester, α-bromopropionic ester, α-bromobutyric ester, α-bromo*iso*butyric ester. The tricarboxylic esters, resulting in this way from the unsubstituted malonic ester, still contain a CH_2-group the hydrogen of which can be replaced with sodium and alkyl iodides. They then yield the same esters which are obtained by starting with the monoalkylmalonic esters.

(2) By the addition of sodium malonic esters to unsaturated carboxylic esters, *e.g.* crotonic ester (Ber. **24**, 2888 : C. 1897, I. 28).

(3) Also, by the gradual saponification of tetracarboxylic esters, containing two carboxyl groups attached to the same carbon atom, which split off carbon dioxide and yield tricarboxylic esters (Ber. **16**, 333 : **23**, 633 : Ann. **214**, 58).

(4) By heating the appropriate ketone-tricarboxylic esters (Ber. **27**, 797), when a loss of·CO occurs.

Like malonic acid, these tricarboxylic acids readily break down with the elimination of CO_2, yielding succinic acids, *e.g.* :



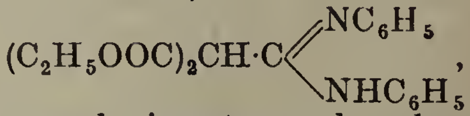
$$\begin{array}{c}(CH_3)_2CCO_2H\\ |\\ CH(CO_2H)_2\end{array} \xrightarrow{-CO_2} \begin{array}{c}(CH_3)_2CCO_2H\\ |\\ CH_2CO_2H\end{array}$$

*iso*Butane-αα*β*-tricarboxylic acid. *as.*-Dimethylsuccinic acid.

For the saponification of tricarboxylic esters consult Ber. **29**, 1867.

Methanetricarboxylic acid, $CH(COOH)_3$. *Ethyl ester*, m.p. 29°, b.p. 253°, from sodiomalonic ester and ethyl chloroformate (Ber. **21**, R. 531). *Methyl ester*, m.p. 46°, b.p. 128°/15 mm., 243°/760 mm. (Ann. **397**, 355).

Alkylmethanetricarboxylic esters, $CR(COOR)_3$, see Ann. **397**, 358.



Methanetricarboxylic diphenylamidine diethyl ester, $(C_2H_5OOC)_2CH{\cdot}C\begin{cases}NC_6H_5\\ NHC_6H_5\end{cases}$, m.p. 167°, is formed by the combination of sodium malonic ester and carbodiphenylimide, $C(NC_6H_5)_2$, (Vol. II) (Ber. **32**, 3176).

Cyanomalonic ester, $CH(CN)(CO_2R)_2$, results from the action of cyanogen chloride on sodium malonic ester. It volatilizes without decomposition under greatly reduced pressure. It has a very acid reaction, and decomposes the alkali carbonates, forming salts, like $CNa(CN)(CO_2R)_2$ (Ber. **22**, R. 567 : C. 1901, I. 675).

Cyanoform, $CH(CN)_3 + CH_3OH$ (?), m.p. 214° (decomp.). Sodium cyanoform is produced when cyanogen chloride acts on malonitrile and sodium ethoxide (Ber. **29**, 1171).

Ethanetricarboxylic ester, carboxysuccinic ester, $C_2H_5OOC{\cdot}CH_2{\cdot}CH(COOC_2H_5)$, b.p. 278°, is obtained from ethyl sodiomalonate and the ester of chloroacetic acid. Chlorine converts it into the *chloro*- compound, $C_2H_2Cl(CO_2C_2H_5)_3$, b.p. 290°. When heated with hydrochloric acid, it yields carbon dioxide, hydrochloric acid, alcohol, and fumaric acid ; when hydrolysed with alkalis, carbon dioxide and malic acid are the products (Ann. **214**, 44).

Methyl α-cyanosuccinate, $(CO_2CH_3)CH_2CH(CN)CO_2CH_3$, is obtained from methyl cyanoacetic ester and chloroacetic ester (Ber. **24**, R. 557).

αβ-Dicyanopropionic ester, $NC{\cdot}CH_2CH(CN)CO_2C_2H_5$, b.p. 169°/20 mm., is prepared from formaldehyde cyanohydrin and sodium cyanoacetic ester :

$$CNCH_2OH + NaCH(CN)CO_2R = CN{\cdot}CH_2CNa(CN)CO_2R + H_2O.$$

The cyanohydrins of homologous aldehydes and ketones condense similarly : *αβ-dicyanoisovaleric ester*, $NC{\cdot}C(CH_3)_2CH(CN)CO_2C_2H_5$, b.p. 150°/22 mm. ; *αβ-dicyanopelargonic ester*, $C_6H_{11}CH(CN)CH(CN)CO_2C_2H_5$, b.p. 192°/20 mm. (C. 1906, II. 1562), etc.

Propane-ααβ-tricarboxylic acid, $CH_3{\cdot}CH(COOH){\cdot}CH(COOH_2)$. The free acid (isomeric with tricarballylic acid), m.p. 146°, breaks down into carbon dioxide and pyrotartaric acid. *Ethyl ester*, b.p. 270°.

Propane-αββ-tricarboxylic ester, $CH_3{\cdot}C(CO_2Et)_2{\cdot}CH_2(CO_2Et)$, b.p. 273°.

Butane-ααβ-tricarboxylic ester, $C_2H_5{\cdot}CH(CO_2Et){\cdot}CH(CO_2Et)_2$, b.p. 278°.

Butane-αββ-tricarboxylic ester, $C_2H_5{\cdot}C(CO_2Et)_2{\cdot}CH_2{\cdot}CO_2Et$, b.p. 281°.

Butane-ααδ-tricarboxylic ester, $(CO_2Et)CH_2CH_2CH_2CH(CO_2Et)_2$, b.p. 203°/40 mm. (C. 1897, II. 542).

iso*Butane-ααβ-tricarboxylic ester*, $(CO_2Et)C(CH_3)_2{\cdot}CH(CO_2Et)_2$, b.p. 277°. (*Cf.* Ber. **23**, 648.)

as.-*Dimethylcyanosuccinic ester*, $CO_2Et{\cdot}CH(CN){\cdot}C(CH_3)_2{\cdot}CO_2Et$, b.p. 186°, is formed from sodium cyanoacetic ester and bromo*iso*butyric ester (Ber. **27**, R. 506 ; C. 1899, I. 593, 873).

α-Cyanoglutaric ester (Ber. **27,** R. 506).

α-Alkyl-α-carboxylglutaric esters (Ann. **292,** 209 : C. 1897, I. 28).

*α-Cyano-β-*iso*propylglutaric ester,* b.p. 195°/30 mm. (C. 1899, I. 1157).

β-Methylpropane-ααγ-tricarboxylic acid, β-methylglutaric-α-carboxylic ester, $(CO_2Et)_2CHCH(CH_3)CH_2CO_2Et$, b.p. 165°/11 mm., is formed from sodium malonic ester and crotonic ester, and gives, somewhat remarkably, a *sodium salt* which, with iodomethane, yields *β-methylbutane-ααγ-tricarboxylic ester,* $(CO_2Et)_2CHCH\cdot(CH_3)CH(CH_3)CO_2Et$, b.p. 167°/10 mm. This substance is isomeric with *β-methylbutane-αγγ-tricarboxylic ester* $(CO_2Et)_2C(CH_3)CH(CH_3)CH_2CO_2Et$, b.p. 161°/10 mm., prepared from sodium methylmalonic ester and crotonic ester. This substance yields a sodium salt which, with iodomethane, gives αβγ-trimethylpropane-ααγ-tricarboxylic acid (Ber. **33,** 3731).

ββ-Dimethyl-α-carboxylglutaric ester, see ββ-dimethylglutaric acid (p. 559).

ββ-Dimethyl-α-cyanoglutaric ester (C. 1899, I. 252, 532).

(*b*) Tricarboxylic Acids with the Carboxyl Groups attached to Three Carbon Atoms

There are many members of this class which are obtained through loss of CO_2 from tetra- and penta-carboxylic acids, which possess one or two pairs of CO_2H-groups attached to the same carbon atom (Ber. **24,** 307, 2889 : **25,** R. 746 : C. 1902, I. 110).

Tricarballylic acid, $CH_2(CO_2H)\cdot CH(CO_2H)\cdot CH_2(CO_2H)$, m.p. 162–164°, occurs in unripe beetroot, and is found in the deposit in the vacuum pans during the manufacture of beet sugar. It is prepared (1) by reduction of aconitic acid (p. 648) (Ann. **314,** 15 : C. 1903, II. 187), and of citric acid (p. 664) ; (2) synthetically from glyceryl tribromide, $CH_2Br\cdot CHBr\cdot CH_2Br$ and KNC, and decomposition of the tricyanide with aqueous potassium hydroxide : also from a whole series of synthetically prepared bodies by cleavage reactions ; (3) from diallylacetic acid (p. 354) by oxidation ; (4) from α-acetyltricarballylic ester (p. 667) by hydrolysis (Ber. **23,** 3756) ; (5) from propane-ααβγ- and -αββγ-tetracarboxylic ester ; (6) from cyanotricarballylic ester, the product of combination of sodium cyanosuccinic ester and bromoacetic ester (C. 1902, I. 409) ; (7) from propane pentacarboxylic ester (p. 678), with loss of CO_2 (Ber. **25,** R. 746). It forms prisms which are easily soluble in water.

The *silver salt,* $C_6H_5O_6Ag_3$; *calcium salt,* $(C_6H_5O_6)_2Ca_3 + 4H_2O$, dissolves with difficulty (C. 1902, I. 409) ; *trimethyl ester,* $C_6H_5O_6(CH_3)_3$, b.p. 150°/13 mm. ; *chloride,* $C_3H_5(COCl)_3$, b.p. 140°/14 mm. (Ber. **22,** 2921) ; *anhydride acid,* $C_5H_6O_5$, m.p. 131° (Ber. **24,** 2890) ; *triamide,* $C_3H_5(CONH_2)_3$, m.p. 206° ; *amidimide,* $C_6H_8O_3N_2$, m.p. 173° (Ber. **24,** 600). *Trihydrazide* and *triazide,* $C_3H_5(CON_3)_3$ (J. pr. Chem. [2] **62,** 235).

Homologous Tricarballylic Acids :

α-Methyl-, two modifications, m.pp. 180° and 134° (*cf.* Monatsh. **23,** 283); *β-methyl-,* m.p. 164° ; *α-ethyl-,* m.p. 147° ; α-n.-*propyl,* m.p. 151° ; α-iso*propyl,* m.p. 161° (Ber. **24,** 288) ; *αα₁-dimethyl-,* three modifications (Ber. **29,** 616) ; *αα-dimethyltricarballylic acid,* three modifications, m.pp. 143°, 174°, and 206° (C. 1899, I. 826 ; 1900, II. 316 ; 1902, I. 409). These acids are prepared from the corresponding cyanotricarballylic acids (the condensation products of sodium cyanosuccinic esters and α-bromo-fatty acid esters), or from sodium cyanoacetic esters and alkylbromosuccinic esters. Trimethyl bromosuccinic ester, however, after reaction with sodium cyanoacetic ester, hydrolysis and cleavage of the product of condensation, does not yield the expected trimethyl tricarballylic acid, but *δ-methylpentane-αγδ-tricarboxylic acid,* $(CH_3)_2C(COOH)CH(COOH)CH_2\cdot CH_2COOH$ (C. 1902, I. 409).

ααβ-Trimethyltricarballylic acid, **camphoronic acid,** $(CH_3)_2C(CO_2H)C(CH_3)\cdot(CO_2H)\cdot CH_2CO_2H$, m.p. 135°, is formed when camphor is oxidized. It is of fundamental importance in the determination of the constitution of camphor (Vol. II).

αβδ-Butanetricarboxylic acid, m.p. 119° (C. 1902, II. 732).

αγδ-Pentanetricarboxylic acid, hæmotricarboxylic acid, two modifications, m.pp. 141° and 175°, is formed by the acid reduction of hæmatinic acid (p. 750) (Ann. **345,** 2).

αγε-Pentanetricarboxylic acid, m.p. 107° (Ber. **24**, 284). *Butane-βδ-dicarboxylic-γ-acetic acid*, $CH_3CH(COOH)CH(CH_2COOH)_2$ (Monatsh. **21**, 879). *Methane-α-tripropionic ester*, $CH[CH(CH_3)CO_2R]_3$, m.p. 201°, is prepared from orthoformic ester, α-bromopropionic ester and zinc (C. 1906, I. 338).

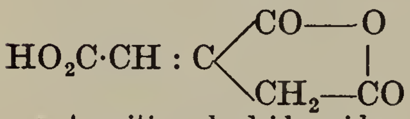
B. OLEFINE TRICARBOXYLIC ACIDS

Aconitic acid, $CH_2(COOH){\cdot}C(COOH):CH(COOH)$, m.p. 191°, with decomposition into CO_2 and itaconic anhydride (p. 571). It is isomeric with trimethylene tricarboxylic acid (*q.v.*), and occurs in different plants; for example, in *Aconitum napellus*, in *Equisetum fluviatile*, in sugar cane, and in beetroots. It is obtained by heating rapidly citric acid alone or with concentrated hydrochloric or sulphuric acid (Ber. **20**, R. 254; Ann. **314**, 15).

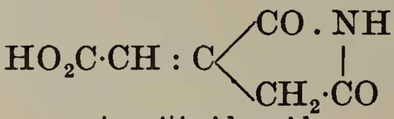
Aconitic acid has been synthetically prepared by the decomposition of oxalocitric lactone ester (*q.v.*) with alkali; by the decomposition of the addition product of sodium malonic ester and acetylenedicarboxylic ester (J. pr. Chem. [2] **49**, 20); also from cyanoaconitic acid, the product of reaction of cyanoacetic ester, oxaloacetic ester and sodium ethoxide (C. 1906, II. 20). It is readily soluble in water, and is reduced by nascent hydrogen to tricarballylic acid.

The *calcium salt*, $(C_6H_3O_6)_2Ca_3 + 6H_2O$, dissolves with difficulty; *trimethyl ester*, $C_6H_3O_6(CH_3)_3$, b.p. 161°/14 mm., results from the distillation of acetylcitric-trimethyl ester (Ber. **18**, 1954), and from aconitic acid, methyl alcohol, and hydrochloric acid (Ber. **21**, 669).

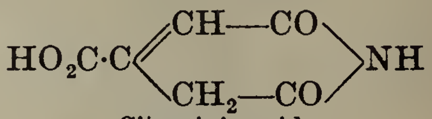
as.-*Aconitic anhydride acid*, $C_6H_4O_5$ (constitutional formula, see below), m.p. 76°, is formed when aconitic acid is heated in vacuo to 140°, and when it is treated with acetyl chloride. When distilled in vacuo it decomposes into CO_2 and itaconic anhydride (Ber. **37**, 3967). as.-*Aconitimide acid*, $C_6H_4O_4(NH)$ (constitutional formula, see below), m.p. 191°, is formed from acyl citrimide esters and alkalis (p. 666); also from β-anilinotricarballylimide esters and dilute hydrochloric acid (Ber. **23**, 3185, 3193). The aconitic esters and ammonia yield the amide of sym.-*aconitimide acid*, *citrazinic acid* (formula, see below) (Vol. II), which results also from the amide of citric acid and mineral acids (Ber. **22**, 1078, 3054: **23**, 831: **27**, 3456):



as.-Aconitic anhydride acid.



as.-Aconitimide acid.



Citrazinic acid.

α-(or γ)-*Methylaconitic acid*, $HO_2C{\cdot}C(CH_3):C(CO_2H)CH_2CO_2H$ or $HO_2C{\cdot}CH{\cdot}{\cdot}CH_2C{\cdot}(CO_2H):CHCO_2H$, m.p. 159°, is prepared from methylcyanoaconitic ester (p. 670). It reacts with acetyl chloride to form an *anhydride acid*, m.p. 51°, which when heated to 159° decomposes into β-methylitaconic anhydride and CO_2. *αγ-Dimethylaconitic acid*, m.p. 164°; the *anhydride-acid*, m.p. 74°, is formed from cyano-αγ-dimethyl-aconitic ester (C. 1906, II. 21).

iso*Aconitic ethyl ester*, $(C_2H_5OOC)_2CHCH:CHCOOC_2H_5$, is formed when dicarboxyglutaconic ester is incompletely hydrolysed. It is converted by piperidine into a bimolecular polymer which yields a *bimeric* glutaconic acid m.p. 207° (p. 576) on hydrolysis with hydrochloric acid (Ber. **34**, 677).

Aceconitic acid and *citracetic acid*, $C_6H_6O_6$, are two acids of unknown constitution, isomeric with aconitic acid. They are obtained by the action of sodium on bromoacetic ester (Ann. **135**, 306: *cf.* Ber. **27**, 3457).

αγδ-Butenetricarboxylic acid, $HOOC{\cdot}CH_2CH(CO_2H)CH:CHCO_2H$, m.p. 148° (C. 1902, II. 732).

Δ^{γ}-Pentene-αγδ-tricarboxylic acid, $HO_2C{\cdot}CH_2CH_2C(CO_2H):CH{\cdot}CO_2H$, is unknown in the free state. Its *anhydride-* and *imide-acid* are identical with the *hœmatinic acids*, obtained from hæmatin (*q.v.*) by the ordinary action of chromic acid. The acids decompose on dry distillation into CO_2 and methylethylmaleic anhydride and imide, respectively (p. 574) (Ann. **345**, 1).

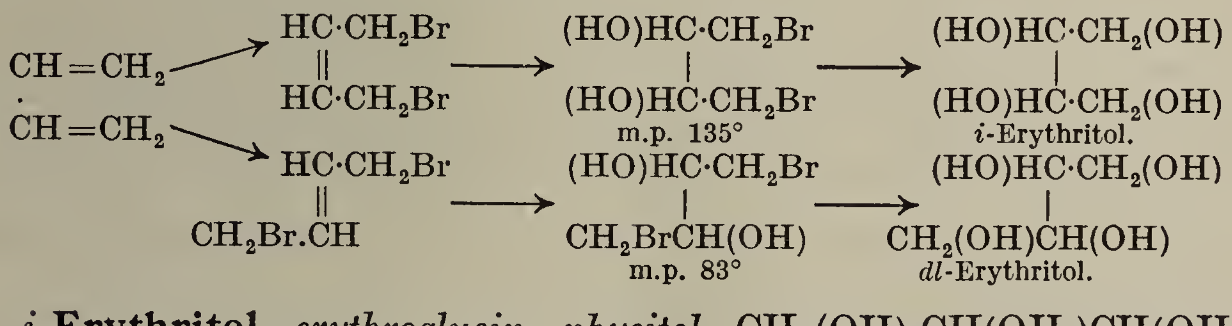
VI. TETRAHYDRIC ALCOHOLS AND THEIR OXIDATION PRODUCTS

Theoretically, there are 15 classes of tetrahydric alcohols, a figure which is obtained by the combination of the individuals —CH_2OH, $=CHOH$, $\equiv COH$, according to the formula, $\frac{m(m+1)(m+2)(m+3)}{1\ .\ 2\ .\ 3\ .\ 4}$, etc., where $m = 3$. The number of possible classes of oxidation products can be calculated by combining the six individuals —CH_2OH, $=CHOH$, $\equiv COH$, —CHO, $=CO$, —CO_2H, substituting $m = 6$ in the above equation and subtracting the number 15 of the tetrahydric alcohols. Thus, it is found that there are 111 classes (126 — 15) of oxidation products theoretically possible. If the difference between the various primary, secondary and tertiary alcohol groups is neglected and, for example, all trihydroxycarboxylic acids are grouped as one class, this number of theoretical classes of oxidation products is reduced to 34. Of these, representatives of some 15 classes are known.

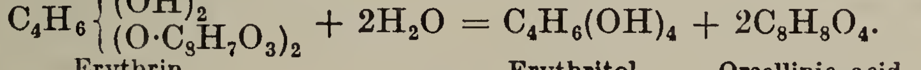
1. TETRAHYDRIC ALCOHOLS

The best-known tetrahydric alcohol is ordinary *i*-erythritol, which, like *meso*tartaric acid (p. 658), is optically inactive by internal compensation. This alcohol and *dl*-erythritol were synthesized from butadiene in 1893 by Griner.

Butadiene (p. 116) forms an unstable dibromide, which becomes rearranged at 100° into two different stable dibromides. When these are oxidized by potassium permanganate, the one passes into the dibromohydrin (m.p. 135°) of ordinary or *i*-erythritol, whilst the other becomes the dibromohydrin (m.p. 83°) of *dl*-erythritol. Potassium hydroxide converts these two dibromohydrins into two butadiene oxides, which, with water, yield respectively *i*- and *dl*-erythritol (Ber. **26,** R. 932 : Ann. **308,** 333) :



i-**Erythritol,** *erythroglucin, phycitol,* $CH_2(OH){\cdot}CH(OH{\cdot})CH(OH){\cdot}$-$CH_2{\cdot}OH$, m.p. 126°, b.p. 330°, occurs free in the alga *Protococcus vulgaris.* It exists as erythrin (orsellinate of erythritol) in many lichens and some algæ, especially in *Roccella Montagnei*, and is obtained from these by hydrolysis with sodium hydroxide or calcium hydroxide.



$$C_4H_6\left\{\begin{matrix}(OH)_2\\(O{\cdot}C_8H_7O_3)_2\end{matrix}\right. + 2H_2O = C_4H_6(OH)_4 + 2C_8H_8O_4.$$

Erythrin. Erythritol. Orsellinic acid.

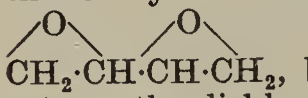
i-Erythritol is also formed by the reduction of *i*-erythrose (Ber. **32,** 3677).

Like all polyhydric alcohols erythritol possesses a sweet taste.

By carefully oxidizing erythritol with dilute nitric acid erythrose results. More intense oxidation produces erythritic acid and *meso*-tartaric acid (p. 658).

i-*Erythritol tetranitrate,* $C_4H_6(ONO_2)_4$, m.p. 61°, explodes violently when struck. It is used medicinally in small doses to reduce high blood pressure. i-*Erythritol tetraacetate,* m.p. 85°.

i-*Erythritol dichlorohydrin,* $C_4H_6(OH)_2Cl_2$, m.p. 125°, is formed from erythritol by the action of concentrated hydrochloric acid. i-*Erythritol ether,* $\overset{O}{\overline{CH_2\cdot CH}}\cdot\overset{O}{\overline{CH\cdot CH_2}}$, b.p. 138°, $D_{18} = 1{\cdot}113$, is formed when potassium hydroxide acts on the dichlorohydrin. It is a liquid with a penetrating odour, and behaves like ethylene oxide (p. 367). It combines slowly with water, yielding erythritol, with 2HCl to the dichlorohydrin, and with 2HNC to the nitrile of dihydroxyadipic acid (Ber. **17,** 1091).



Condensation Products.—Erythritol condenses with formaldehyde, benzaldehyde and acetone under the action of hydrochloric acid yielding i-*erythritol diformal,* $C_4H_6O_4(CH_2)_2$, m.p. 96° (Ann. **289,** 27) ; i-*erythritol dibenzal,* m.p. 97° ; and i-*erythritol diacetone,* $C_4H_6O_4(C_3H_6)_2$, m.p. 56°, b.p. 105°/29 mm. (Ber. **28,** 2531).

d-**Erythritol,** m.p. 88°, $[\alpha]_D = -4{\cdot}4°$, is obtained by the reduction of erythrulose (C. 1900, II. 31). *l*-**Erythritol,** $[\alpha]_D = +4{\cdot}3°$, is similarly obtained from *l*-threose (C. 1901, II. 179).

dl-**Erythritol,** m.p. 72°, is obtained by the combination of the *d*- and *l*-compounds. It is identical with the substance obtained from divinyl (p. 116). dl-*Erythritol ether* (Ber. **26,** R. 932). *Tetraacetyl*-dl-*erythritol,* m.p. 53°.

Nitro-*tert.*-butylglycerol, $NO_2C(CH_2OH)_3$, m.p. 158°, is formed from nitromethane, formaldehyde, and potassium hydrogen carbonate (Ber. **28,** R. 774). Reduction converts it into *hydroxylamino*-tert.-*butylglycerol,* $HOHN\cdot C(CH_2OH)_3$, m.p. 140° (Ber. **30,** 3161), which by the action of mercuric oxide is converted into the oxime of dihydroxyacetone (p. 590).

Pentaerythritol, $C(CH_2OH)_4$, m.p. 250–255°, is obtained by condensing formaldehyde and acetaldehyde by means of lime (Compt. rend. **133,** 590 : see also vinyl*cyclo*propane, Vol. II). *Tetraacetate,* m.p. 84° (Ann. **276,** 58). *Disulphite,* m.p. 153° (Ber. **61,** 118). *Tetraethyl ether,* b.p. 220° (C. 1897, II. 694). The *mono*- and *di-formaldehyde* condensation products, m.p. 60° and 50° (Ber. **61,** 55), the *mono*- and *diacetone* compounds, m.p. 135° and 117° (Ber. **61,** 116), and the *dibenzylidine* compound, m.p. 160° (Ann. **289,** 21), are obtained from the appropriate aldehyde or ketone and pentaerythritol in presence of hydrochloric acid or anhydrous copper sulphate.

According to recent investigations (Z. anorg. Chem. **172,** 121) the central atom in pentaerythritol, contrary to previous views (Ber. **59,** 1526), possesses a tetrahedral configuration, in agreement with van 't Hoff's representation.

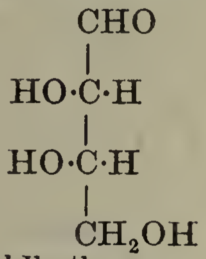
Two **hexaerythritols** have been prepared by oxidizing diallyl, $CH_2{=}CH\cdot CH_2{-}CH_2{-}CH{=}CH_2$ (p. 117). Oxidation of hexadiene dibromide, $CH_3CHBrCH{:}CHCHBrCH_3$, produces a dibromo-di-hydroxyhexane which, when warmed with aqueous sodium hydroxide, yields *hexadiene dioxide,* $\overline{O\cdot CH(CH_3)CH}\cdot\overline{CH\cdot CH\cdot CH(CH_3)\cdot O}$, b.p. 177° (Ber. **35,** 1341).

2. TRIHYDROXYALDEHYDES and

3. TRIHYDROXYKETONES

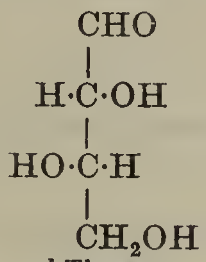
Erythrose, *tetrose,* is probably a mixture of a trihydroxyaldehyde and a trihydroxyketone (*cf.* Glycerose, p. 589 : Ber. **35,** 2627). It is produced when erythritol is oxidized with dilute nitric acid. It yields *phenylerythrosazone,*

$C_4H_6O_2(N_2HC_6H_5)_2$, m.p. 167° (Ber. **20**, 1090). This probably is also produced from the condensation product of glycolyl aldehyde (p. 389) (Ber. **25**, 2553 : **35**, 2630).



$$\begin{array}{c} CHO \\ | \\ HO\cdot C\cdot H \\ | \\ HO\cdot C\cdot H \\ | \\ CH_2OH \end{array}$$

l-Erythrose
(I)



$$\begin{array}{c} CHO \\ | \\ H\cdot C\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ CH_2OH \end{array}$$

l-Threose
(II)

d-**Erythrose** (*lævo-rotatory*) is formed when *d*-arabonic acid is oxidized with hydrogen peroxide (Ber. **32**, 3674). *l*-**Erythrose** [(I) above] (*dextrorotatory*) results from the oxidation of *l*-arabonic acid, or by the decomposition of *l*-arabinose oxime through the nitrile, by loss of hydrocyanic acid (Ber. **32**, 3666 : **34**, 1365) (*cf.* also the decomposition of *d*-dextrose, p. 673). Similarly, by oxidation, or by the hydrocyanic acid reaction, *l*-xylose yields *l*-**threose** [(II) above] stereoisomeric with erythrose. *l*-Erythritose and *l*-threose yield the same osazone (Ber. **34**, 1370).

Erythrulose is obtained from erythritol by means of the *Sorbose bacterium.* It yields *d*-erythritol on reduction, and is probably a ketose. **Methyltetrose,** $CH_3[CHOH]_3CHO$, is obtained from rhamnose oxime and acetic anhydride, and also from rhamnonic acid and hydrogen peroxide. *Osazone,* m.p. 173°. *Benzylphenylhydrazone,* m.p. 97°, when oxidized with nitric acid, yields *d*-tartaric acid ; bromine water produces methyltetronic acid (Ber. **29**, 138 : **35**, 2360).

Thyminose, $CH_2OH\cdot[CHOH]_2\cdot CH_2\cdot CHO$, is a desoxyribose occurring in animal nucleic acids. (J. Biol. Chem. **83**, 793, 803 : **85**, 785.)

4. DIHYDROXYDIALDEHYDES

Mesotartaric aldehyde, $CHO\cdot CHOH\cdot CHOH\cdot CHO$, is obtained as a colourless powder by the action of dilute sulphuric acid on its acetal. The *acetal* is prepared by the oxidation of maleinaldehyde diacetal, the reduction product of acetylenedialdehyde diacetal, with permanganate (Ber. **45**, 322).

l-*Tartaric aldehyde* is obtained from the diamide of saccharic acid, bromine and alkali (p. 717).

5. HYDROXYTRIKETONES

γ-Methylheptan-γ-ol-βεζ-trione, $CH_3\cdot CO\cdot CMe(OH)\cdot CH_2\cdot CO\cdot CO\cdot CH_3$, b.p. 128°/18 mm., is the aldol of diacetyl (p. 402).

6. TETRAKETONES

Tetraacetylethane, $(CH_3CO)_2CH—CH(COCH_3)_2$, is obtained from sodium acetylacetone by means of iodine or by electrolysis (p. 403).

Octane-βδεη-tetraone, oxalyldiacetone, $CH_3COCH_2\cdot COCO\cdot CH_2COCH_3$, m.p. 121°, and *oxalyldimethylethyl ketone, decane-γεζθ-tetraone,* $C_2H_5COCH_2\cdot COCO\cdot CH_2\text{-}COC_2H_5$, m.p. 76°, are formed from oxalic ester, acetone or methylethyl ketone and sodium ethoxide. They consist of yellow crystals, which remain yellow on fusion and form yellow solutions. Oxalyl diacetone give a dipyrazole derivative with phenylhydrazine (Ann. **278**, 294).

Methenylbisacetylacetone, $(CH_3CO)_2CH\cdot CH{=}C(COCH_3)_2$ is obtained from ethoxymethyleneacetylacetone (p. 592) by the addition of acetylacetone.

7. TRIHYDROXYMONOCARBOXYLIC ACIDS

Trihydroxybutyric acid, rac.-*erythronic acid, erythroglucic acid,* $CH_2OH\text{-}[CHOH]_2CO_2H$, is obtained by the oxidation of erythrytol (Ber. **19**, 468). It is a crystalline deliquescent mass.

d-*Erythronic acid* (lævorotatory) is formed by the oxidation of *d*-erythritose with bromine ; from *d*-fructose with HgO ; and from dextrosone (p. 686) with bromine (C. 1902, I. 859 : II. 109). d-*Erythronic lactone,* m.p. 103°.

l-*Erythronic acid* (dextrorotatory) is prepared from *l*-erythrose and bromine water. l-*Erythronic lactone*, m.p. 104° (Ber. **34**, 1362).

rac.-*Erythronic lactone*, m.p. 91°, is obtained from γ-hydroxycrotonic lactone (p. 453), and permanganate. The *γ-ethyl ether* of erythronic acid, $C_2H_5O\cdot CH_2CH\text{-}OH\cdot CHOH\cdot CO_2H$, m.p. 91°, is similarly obtained from γ-ethoxycrotonic acid (C. 1905, I. 1138 : II. 457).

Trihydroxy*iso*butyric acid, $(CH_2OH)_2\cdot C(OH)CO_2H$, m.p. 116°, is obtained from glycerose and HNC (Ber. **22**, 106).

αβγ-Trihydroxyvaleric acid, *αβ-dihydroxy-γ-valerolactone*, $CH_3CHCH(OH)\text{-}CH(OH)COO$, m.p. 100°, is formed by oxidation of α-angelic acid lactone (p. 453) by permanganate (Ann. **319**, 194). This dihydroxyvalerolactone must be looked on as being the racemic form of the *methyltetronic acid lactone*, m.p. 121°, $[\alpha]_D = -47\cdot5°$, obtained by oxidation of methyltetrose (p. 651) by bromine water. αβγ-Trihydroxyvaleric acid is specially characterized by its *phenylhydrazide*, m.p. 169°, and its *brucine salt* (Ber. **35**, 2365).

αγδ-Trihydroxyvaleric acid ; the *αδ-oxide* of this acid, the 4-*hydroxytetrahydrofuran*-2-*carboxylic acid*, $OCH_2\cdot CH(OH)CH_2CHCOOH$, m.p. 110°, is formed from the corresponding malonic acid derivative when it is heated with water (Ber. **37**, 4544).

The corresponding αδ-imide—4-*hydroxypyrrolidine*-2-*carboxylic acid*, **β-hydroxyproline**, $HNCH_2CH(OH)CH_2CHCO_2H$, α-form, m.p. 261° (decomp.), β-form 250° (decomp.), is formed from αδ-bromo-chloro-γ-valerolactone, $ClCH_2\text{-}CH\cdot CH_2\cdot CHBr\cdot COO$. The α-form yields a slightly soluble copper salt. This acid, like the αδ-oxide, is prepared from synthetic δ-chlorovalerolactonecarboxylic ester (see p. 653) by the action of ammonia. Two inactive forms are produced, one of which can be resolved by the aid of quinine with the formation of the natural *hydroxyproline*, m.p. 270° (decomp.) $[\alpha]_D^{20}$, $-81\cdot04°$, which is also prepared by the hydrolysis of gelatin (Ber. **35**, 2660).

Both compounds possess a sweet taste, are reduced by hydriodic acid and phosphorus to proline (p. 598), and are very stable towards hydrolytic agents (Ber. **41**, 1726).

8. DIHYDROXYKETOMONOCARBOXYLIC ACIDS

αγ-Diethoxy-acetoacetic ester, $C_2H_5O\cdot CH_2CO\cdot CH(OC_2H_5)\cdot CO_2C_2H_5$, b.p. 132°/14 mm., is prepared from ethoxychloroacetoacetic ester (p. 600) and sodium ethoxide (Ann. **269**, 28).

9. HYDROXYDIKETOCARBOXYLIC ACIDS

Acetylacetone chloral, $CCl_3\cdot CH(OH)CH_2CO\cdot CH_2COCH_3$, m.p. 78°, is a derivative of α-hydroxy-γε-diketoheptoic acid. It is prepared from chloral and acetylacetone (C. 1898, II. 704).

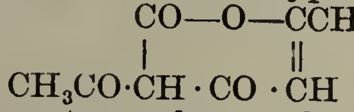
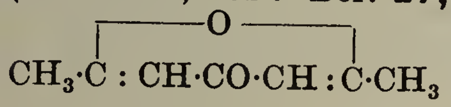
10. TRIKETOMONOCARBOXYLIC ACIDS

The *β-phenylhydrazone* of *αβγ-triketo*-n.-*valeric acid*, m.p. 206°, is prepared from sodium acetoneoxalic acid and diazobenzene chloride (Ann. **278**, 285).

Diacetylpyroracemic acid, $(CH_3CO)_2CHCOCO_2H$, provides a derivative *cyanoiminomethylacetylacetone* $(CH_3CO)_2CH\cdot C(NH)CN$, which is prepared from acetylacetone, cyanogen and a little sodium ethoxide. Aqueous sodium hydroxide decomposes it into sodium cyanide and cyanoacetylacetone (p. 603). It combines with a further quantity of acetylacetone to form dicyanodiacetylacetone and similarly with acetoacetic ester and malonic ester (Ann. **332**, 146).

Derivatives of *pyruvylpyruvic acid*, $CH_3COCO\cdot CH_2COCOOH$, are formed from pyroracemic ester and aromatic amines, *e.g.*, $CH_3C(NC_6H_5)COCH_2C(NC_6H_5)CO_2\text{-}C_2H_5$, which is decomposed by sulphuric acid into $CH_3C(NC_6H_5)COCH_2COCO_2\text{-}C_2H_5$, m.p. 140° (C. 1902, I. 1320). *Homopyruvylpyruvic acid*, αγδ-triketoheptoic acid, provides derivatives such as the *methoxime ester*, $C_2H_5C(NO\cdot CH_3)COCH_2\text{-}$

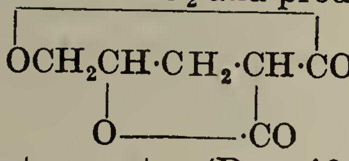
$COCO_2R$; *methyl ester*, m.p. 80° ; *ethyl ester*, m.p. 41°, which are prepared from the methoxime of acetylpropionyl (pp. 402, 407), oxalic ester, and sodium ethoxide (Ber. **38**, 1917).

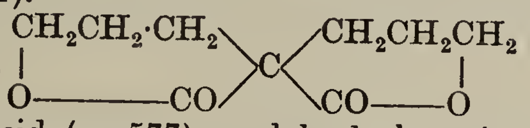
αγ-Diacetylacetoacetic acid, $CH_3COCH_2COCH(COCH_3)CO_2H$. The lactone of the δ-*aci*- or -enol-form of this hypothetical acid, *dehydracetic acid*, 6-*methyl*-3-*aceto-pyronone*,  $\begin{array}{l}\quad\;\; CO—O—CCH_3 \\ \quad\;\; | \qquad\quad \Vert \\ CH_3CO\cdot CH\cdot CO\cdot CH\end{array}$, m.p. 108°, b.p. 269°, is formed by boiling acetoacetic ester under a reflux condenser ; from dehydracetocarboxylic acid (Ann. **273**, 186) by evaporation with aqueous sodium hydroxide ; from acetyl chloride and pyridine ; and from triacetic acid (p. 603) by heating with acetic anhydride and sulphuric acid (C. 1900, II. 625). It is isomeric with *iso*dehydracetic acid (p. 626). The constitution of dehydracetic acid has been demonstrated by *Feist* (Ann. **257**, 261 : Ber. **27**, R. 417). Hydriodic acid produces dimethylpyrone,  $CH_3\cdot\overbrace{C : CH\cdot CO\cdot CH : C}^{O}\cdot CH_3$ (*q.v.*).

11. DIHYDROXYDICARBOXYLIC ACIDS

(i) SATURATED DIHYDROXYDICARBOXYLIC ACIDS

A. Malonic Acid Derivatives

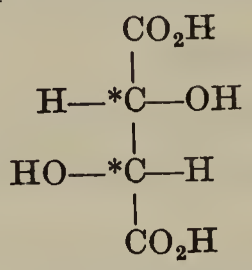
γδ-Dihydroxypropylmalonic acid, $CH_2(OH)CH(OH)CH_2CH(CO_2H)_2$; *lactone ester*, *δ-hydroxy-γ-valerolactone-α-carboxylic ester*, $CH_2(OH)\cdot\overline{CHCH_2CH(CO_2C_2H_5)\text{-}COO}$, a syrup, is formed from δ-chloro-γ-valerolactone carboxylic ester, the product of condensation of epichlorohydrin (p. 587) and malonic ester. The lactone ester and alcoholic ammonia form *γδ-dihydroxypropylmalonamide*, m.p. 140° (Ber. **35**, 197 : *cf.* also Ber. **38**, 1939). Hydrolysis of the chlorovalerolactone ester causes loss of CO_2 and production of chloro-γ-valerolactone, together with the *dilactone*,  $\begin{array}{l}\overline{OCH_2CH\cdot CH_2\cdot CH\cdot CO}\\ \qquad\quad\;\, | \qquad\quad\;\; | \\ \qquad\quad\;\, O\text{———}\cdot CO\end{array}$, m.p. 180° ; bromine produces α-bromo-δ-chloro-γ-valerolactone ester (Ber. **40**, 301).

Di-ω-hydroxypropylmalonic acid dilactone,  $\begin{array}{l}CH_2CH_2\cdot CH_2\\ |\\ O\text{————}CO\end{array}\!\!>C<\!\!\begin{array}{l}CH_2CH_2CH_2\\ \qquad\qquad\; |\\ CO\text{——}O\end{array}$, m.p. 106°, is formed from diallylmalonic acid (p. 577), and hydrobromic acid (Ann. **216**, 67).

B. Succinic Acid Derivatives

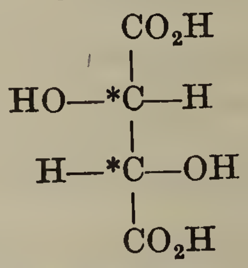
Tartaric Acids, *Dihydroxysuccinic Acids*.—Tartaric acid is known in four modifications ; all possess the same structure and can be converted into one another. They are : (1) Ordinary or *dextro*-tartaric acid. (2) *Lævo*-tartaric acid. These two are distinguished from each other by their equally great but opposite molecular rotatory power. (3) *Racemic acid*, paratartaric acid, or *dl*-tartaric acid. This is optically inactive, but can be resolved into dextro- and lævo-tartaric acids, from which it can again be reproduced by their union. (4) *meso*Tartaric acid, antitartaric acid, *i*-tartaric acid, is optically inactive and cannot be split into other forms. The isomerism of these four acids was exhaustively considered in the introduction. According to the theory of *van 't Hoff* and *Le Bel*, it is attributable to the presence of two asymmetric carbon atoms in the dihydroxysuccinic acids. A compound containing one asymmetric carbon atom may occur in three modifications—a dextro-form, a lævo-form, and, by union of these two, an inactive, resolvable *dl*-modification. If the same atoms or atomic groups are joined to two asymmetric carbon atoms,—that is, if the compound be symmetrically constructed, like dihydroxysuccinic acid,—then in addition to the three modifications capable of forming a compound with one asymmetric carbon atom there arises a fourth possibility. Should the groups linked to the one asymmetric carbon atom (viewed from the point of union of the two asymmetric carbon atoms) show an opposite arrangement from that of the groups attached to the second asymmetric carbon atom, then an inactive body will result by virtue of *internal compensation.* The action on polarized light occasioned by the one asymmetric carbon atom is equalized by an equally great but oppositely directed influence exerted by the second asymmetric carbon atom. (See also Ber. **35**, 4344.)

Therefore, the four symmetrical dihydroxysuccinic acids can be represented by the following formulæ, which represent the projection of the spacial formulæ on the plane of the paper.



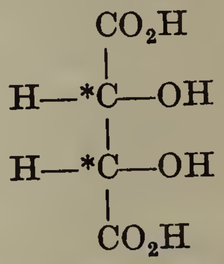
$$\begin{array}{c} CO_2H \\ | \\ H—{}^*C—OH \\ | \\ HO—{}^*C—H \\ | \\ CO_2H \end{array}$$

(1) *dextro*Tartaric acid.



$$\begin{array}{c} CO_2H \\ | \\ HO—{}^*C—H \\ | \\ H—{}^*C—OH \\ | \\ CO_2H \end{array}$$

(2) *lævo*Tartaric acid.



$$\begin{array}{c} CO_2H \\ | \\ H—{}^*C—OH \\ | \\ H—{}^*C—OH \\ | \\ CO_2H \end{array}$$

(3) *meso*Tartaric acid.

d-Tartaric acid + *l*-tartaric acid = (4) Racemic acid.

The configuration of *d*-tartaric acid, as represented above, follows in consequence of the formation of this acid from the oxidation of methyltetrose, the decomposition product of rhamnose (p. 675).

The heat of combustion of the ester of *meso*tartaric acid is 2·6 Cal. greater than that of racemic ester (C. 1919, III. 778): this difference between the *meso-* and *racemic* forms appears to a general phenomenon (C. 1926, II. 2537).

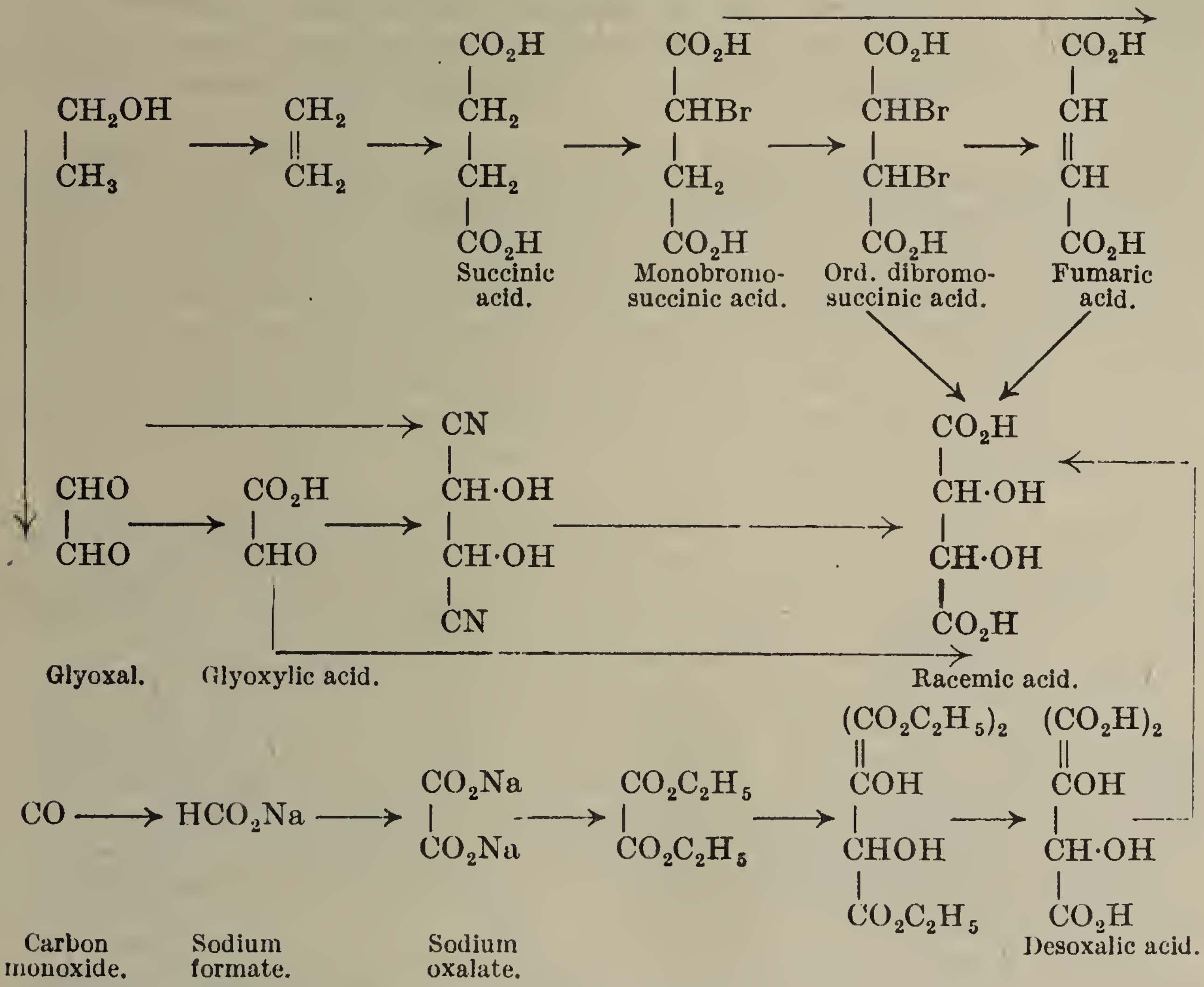
Historical.—*Scheele* in 1769 showed how this acid could be isolated from argol. *Kestner* in 1822 discovered racemic acid as a by-product in the manufacture of ordinary tartaric acid, and in 1826 *Gay-Lussac* investigated the two acids. He and later *Berzelius* (1830) proved that ordinary tartaric acid and racemic acid possessed the same composition, and this fact led Berzelius to introduce the term isomerism into chemical science (p. 34). *Biot* (1838) showed that a solution of ordinary tartaric acid rotated the plane of polarized light to the right, whereas the solution of racemic acid proved to be optically inactive, and was without action upon the polarized ray. *Pasteur's* classic investigations (1848–1853) demonstrated that racemic acid could be resolved into *dextro-* and *lævo*-tartaric acid, and be again re-formed from them. In addition to *lævo*-tartaric acid, Pasteur also discovered inactive or *meso*tartaric acid, which cannot be resolved. *Kekulé* in 1861 and, independently of him, *Perkin, Sr.*, and *Duppa* synthesized racemic acid and *meso*tartaric acid from succinic acid, derived from amber, through the ordinary dibromosuccinic acid. In 1873 *Jungfleisch* obtained racemic acid and *meso*tartaric acid from synthetic succinic acid, and also the other two tartaric acids derivable from racemic acid. *Van 't Hoff* in 1874 and, independently of him, *Le Bel* referred the isomerism of the four tartaric acids to the presence of two asymmetric carbon atoms in symmetrical dihydroxysuccinic acid. In 1880 and 1881 *Kekulé* and *Anschütz* found that racemic acid was obtained from fumaric acid and *meso*tartaric acid from maleic acid, by oxidation with permanganate. This reaction directly linked the isomerism of the tartaric acids to the isomerism of the two unsaturated acids—fumaric acid and maleic acid.

(1) **Racemic acid,** *paratartaric acid,* $C_4H_6O_6 + H_2O$, m.p. 206° (decomp.) (anhydrous), is sometimes found in conjunction with tartaric acid in the juice of the grape, and is formed in the preparation of ordinary tartaric acid, when the solution is evaporated over a flame, especially in the presence of alumina.

Racemic acid appears (1) in the oxidation of mannitol, dulcitol and mucic acid with nitric acid, as well as when fumaric acid (Ber. **13,** 2150), sorbic acid, and piperic acid are oxidized by potassium permanganate (Ber. **23,** 2772). It is synthetically obtained (2) from glyoxal by means of hydrocyanic and hydrochloric acids (together with *meso*tartaric acid, Ber. **27,** R. 749), and (3) from *iso*dibromo- and (together with *meso*tartaric acid) from dibromosuccinic acid, by the action of silver oxide (p. 556); (4) together with glycollic acid (*cf.* the pinacone formation, p. 360), when glyoxylic acid is reduced with acetic acid and zinc; (5) by heating desoxalic acid, $COOH\cdot CHOH\cdot C(OH)(COOH)_2$ (p. 678), with water to 100°, when carbon dioxide is split off.

Ethyl alcohol, which can be synthesized in various ways, constitutes the parent substance for the first four syntheses. In the fifth synthesis carbon monoxide serves for that purpose.

Synthesis of Racemic Acid



Racemic acid is also produced when equal quantities of concentrated solutions of *d*- and *l*-tartaric acids are mixed (Ber. **25,** 1566), and together with *meso*tartaric acid when ordinary tartaric acid is heated with water to 175°.

Properties.—Racemic acid crystallizes in rhombic prisms which slowly effloresce in dry air. It is less soluble (1 part in 5·8 parts at

15°) in water than the tartaric acid, and has no effect on polarized light. Potassium permanganate oxidizes it to oxalic acid, and hydriodic acid reduces it to inactive malic and succinic acids.

Its *salts* closely resemble those of tartaric acid, but do not show hemihedral faces ; the acid *potassium salt* is appreciably more soluble than cream of tartar ; *calcium salt,* $C_4H_4O_6Ca + 4H_2O$, dissolves with more difficulty than the corresponding salts of three other tartaric acids. Dilute acetic acid and ammonium chloride do not dissolve it. It is formed on mixing solutions of calcium *d*- and *l*- tartrates ; *barium salt,* $C_4H_4O_6Ba + 2\frac{1}{2}H_2O$, or $5H_2O$ (Ann. **292, 311**). Racemic changes of the racemates (Ber. **32,** 50, 857).

Optical Resolution of Racemic Acid.—When Pasteur was studying racemic acid he discovered methods for the decomposition of optically inactive bodies into their optically active components, which were briefly considered in the introduction (p. 72) :

(1) *Penicillium glaucum,* growing in a racemic acid solution, destroys the *dextro*-tartaric acid, leaving the *l*-tartaric acid unattacked.

(2*a*) From a solution of sodium ammonium racemate the unaltered salt, without hemihedral faces, separates above + 28° (Ber. **29,** R. 112). When the crystallization takes place below + 28°, large rhombic crystals form, some of which show right, others left hemihedral faces. The similar forms can be separated by hand, and by comparing a solution of the crystals with a solution of calcium *dextro*-tartrate (Ann. **226,** 193), the former will be found to possess *dextro*-rotatory power and yield common tartaric acid, whereas the latter yield the *lævo*-acid.

(2*b*) A solution of cinchonine racemate yields, on the first crystallization, the more sparingly soluble *lævo*-tartrate. If only half as much cinchonine, as is necessary for the production of the acid salt, be introduced, then two-thirds of the calculated quantity of cinchonine *lævo*-tartrate will separate (Ber. **29,** 42). Quinicine *dextro*-tartrate is the first to crystallize from a solution of quinicine racemate.

(3) Racemic acid may also be resolved by means of its *l*-bornyl hydrogen ester (J.C.S. **117,** 191).

Esters of Racemic Acid : Dimethyl ester, m.p. 85°, b.p. 282°, is produced from racemic acid, methyl alcohol, and HCl. It can be made by fusing together the dimethyl ester of *d*- and *l*-tartaric acids. It is obtained pure by distillation under reduced pressure. In vapour form it dissociates into the dimethyl ester of the *d*- and *l*-tartaric acids (Ber. **18,** 1397 : **21,** R. 643).

Diacetylracemic anhydride, $(C_2H_3O_2)_2C_4H_2O_3$, m.p. 123° (Ber. **13,** 1178). *Diacetylracemic dimethyl ester,* $(C_2H_3O_2)_2C_4H_2O_4(CH_3)_2$, m.p. 86°, results from the action of acetyl chloride on the dimethyl ester ; and upon evaporating the benzene solution of the dimethyl *l*- and *d*-diacetyl tartaric esters (Ann. **247,** 115). *Nitrile of diacetylracemic acid,* $CH_3CO{\cdot}OCH(CN){\cdot}CH(CN)O{\cdot}COCH_3$, m.p. 97°, is produced together with the nitrile of diacetyl*meso*tartaric acid, when acetic anhydride acts on the liquid portion of the additive product resulting from HNC and glyoxal in alcohol (Ber. **27,** R. 749).

Imides : Methyl-, ethyl-, and *phenyl-imides,* m.p. 157°, 179°, and 235° (Ber. **30,** 3040). The *anil* of *diacetylracemic acid,* m.p. 94°, results when PCl_5 acts on the anilic acid, and when the *anils* of d- and l-*diacetyltartaric acids,* m.p. 126°, combine (privately communicated by *Anschütz* and *Reitter*).

(2) *Dextro-rotatory* or *ordinary* **tartaric acid** (*Acidum tartaricum*), m.p. 167–170° (Ber. **22,** 1814), is widely distributed in the vegetable

world, and occurs principally in the juice of the grape, from which it deposits after fermentation in the form of potassium hydrogen tartrate (argol). It results on oxidizing methyltetrose, saccharic acid, and lactose with nitric acid.

Ordinary tartaric acid crystallizes in large monoclinic prisms, which dissolve readily in water (1 part in 0·76 part at 15°) and alcohol, but not in ether. Its solution rotates the ray of polarized light to the right, but a very concentrated aqueous solution at low temperatures turns it to the left (Ber. **32**, 1180). When it is heated with water to 165° it changes mainly to *meso*tartaric acid ; at 175° the racemic acid predominates. Also, boiling with concentrated aqueous alkali converts *d*-tartaric acid partially into racemic and *meso*tartaric acids (Ber. **30**, 1574). It also forms racemic acid when it is brought together with a concentrated solution of *l*-tartaric acid.

On dry distillation it yields pyrotartaric acid and pyruvic acid (Intermediate stages of this reaction, see J.C.S. **119**, 34).

When carefully oxidized, *d*-tartaric acid yields dihydroxymaleic acid (p. 661), dihydroxytartaric acid, and tartronic acid (p. 604) ; stronger oxidizing agents decompose it into carbon dioxide and formic acid.

Hydriodic acid reduces it to *d*-malic and succinic acids.

d-Tartaric acid is applied in dyeing or colouring, as an ingredient of effervescing powders, and as a medicine. Nearly all of its salts meet with extended uses.

Salts. Tartrates.—The *normal potassium salt*, $C_4H_4O_6K_2 + \frac{1}{2}H_2O$, is readily soluble in water ; from it acids precipitate the salt, $C_4H_5O_6K$, which is not very soluble in water, and constitutes natural *argol* (*Cremor tartari*) ; **Rochelle salt,** *potassium sodium tartrate*, $C_4H_4O_6KNa + 4H_2O$ (*Seignette salt*), crystallizes in large rhombic prisms with hemihedral faces ; *sodium ammonium salt*, $C_4H_4O_6Na(NH_4) + 4H_2O$, is obtained from sodium ammonium racemate ; *calcium salt*, $C_4H_4O_6Ca + H_2O$, is precipitated from solutions of normal tartrates, by calcium chloride, as an insoluble, crystalline powder. It dissolves in acids and alkalis, and is reprecipitated from alkaline solution as a jelly on boiling—a reaction serving to distinguish tartaric from other acids. (See also Calcium racemate.)

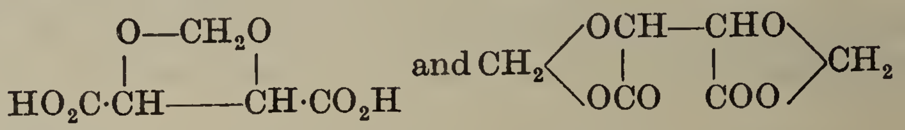
Lead salt, $C_4H_4O_6Pb$. *Copper salts* are not precipitated by alkali hydroxides in presence of tartaric acid. When cupric hydroxide is dissolved in tartaric acid and aqueous alkali, double salts are formed, such as cupric sodium ditartrate, $C_4H_2O_6CuNa_2 + C_4H_2O_6Na_4 + 13H_2O$ (Ber. **32**, 2347). A solution of copper sulphate, rochelle salt, and sodium hydroxide is known as *Fehling's solution*, and is employed in the quantitative analysis of certain sugars (p. 685).

Tartar Emetic.—*Potassium antimonyl tartrate*, $COOK\cdot CHOH\cdot CHOH\cdot COOSbO + \frac{1}{2}H_2O$, or $C_4H_4O_6 : SbOK + \frac{1}{2}H_2O$, or $CO_2K[CHOH]_2COOSb\left<\begin{matrix}O\\O\end{matrix}\right>Sb\cdot OCO[CHOH]_2\cdot COOK + H_2O$ (Ber. **16**, 2386), is prepared by boiling cream of tartar with antimony oxide and water. It crystallizes in rhombic octahedra, which slowly lose their water of crystallization on exposure and fall to a powder. It is soluble in fourteen parts of water at 10°. Its solution possesses an unpleasant metallic taste, and acts as an emetic. See Ber. **29**, R. 84 : **28**, R. 463, for the corresponding arsenic compound.

dextro-*Tartaric acid esters*, $ROOC\cdot CH(OH)CH(OH)\cdot COOR$ (*cf.* Racemic esters), are obtained as follows : the acid is dissolved in methyl or ethyl alcohol, hydrochloric acid gas is passed through the solution, and the liquid is distilled under diminished pressure. PCl_5 converts them into esters of chloromalic acid (p. 659) and chlorofumaric acid. The esters constitute the first homologous series of optically active substances, of which the rotation of the plane of polarized light was investigated (*Anschütz* and *Pictet*, Ber. **13**, 1177 : *cf.* Ber. **27**, R. 511, 621, 725, 729 : Ber. **28**, R. 148 : C. 1898, II. 17). *Dimethyl ester*, m.p. 48°, b.p. 280°/760 mm. $[\alpha]_D^{20} = +2{\cdot}16$. *Diethyl ester*, fluid, b.p. 280°/760 mm. $[\alpha]_D^{20} = +7{\cdot}66$. *Di-n.-propyl ester*, fluid, b.p. 303°/760 mm. $[\alpha]_D^{20} = +12{\cdot}44$.

Ethers are formed by the action of silver oxide and alkyl iodides on the tartaric esters. Thus methyl *d*-tartrate yields *methyl* d-*dimethoxysuccinate*, $Me_3OCO{\cdot}CH(OMe){\cdot}CH(OMe){\cdot}COOMe$, m.p. 51°, b.p. 132°/12 mm., which on hydrolysis yields *dimethoxysuccinic acid*, m.p. 151°. The ethers are also obtained by the action of alkyl iodides on silver tartrate. If sodium ethoxide is used in the reaction between alkyl iodides and tartaric esters there results a mixture of *sym.*- and *as.*-dialkoxysuccinic esters (p. 621), which can also be produced by the action of sodium ethoxide on *sym.*-dibromosuccinic ester (C. 1900, I. 404 : 1901, II. 401).

Mono- and *Di-formal Tartaric Acids :*



(C. 1903, I. 136).

Diacetyl-d-*tartaric anhydride*, $(C_2H_3O)_2C_4H_2O_3$, m.p. 135°, is prepared by treatment of tartaric acid with acetic anhydride and a little sulphuric acid. Pyridine acetate at 0° produces the pyridine salt of hydroxymaleic anhydride (p. 620). *Diacetyltartaric dimethyl ester*, m.p. 103°. *Diacetyltartaric dianilide*, m.p. 214° (Ann. **279**, 138). *Diacetyl*-d-*tartaric anil* ; see Diacetyl racemic anil (p. 656). Other imides (Ber. **29**, 2710).

Tartaric hydrazide, m.p. 183° : *tartaric azide*, from the hydrazide and nitrous acid, m.p. 66° (J. pr. Chem. **95**, 214).

Nitrotartaric acid, *dinitrotartaric acid*, $(NO_2O)_2C_2H_2(CO_2H)_2$, is obtained from tartaric acid by the action of nitric and sulphuric acids (J.A.C.S. **43**, 577). It dissolves readily in alcohol and ether, and is insoluble in benzene and chloroform. $[\alpha]_D^{20} = +13{\cdot}5°$ in methyl alcohol. In aqueous solution the substance decomposes into dihydroxytartaric acid (p. 662), $CO_2H{\cdot}C(OH)_2{\cdot}C(OH)_2CO_2H$, which breaks down further into CO_2 and tartronic acid. *Dinitrotartaric esters : Dimethyl ester*, m.p. 75° ; *diethyl ester*, m.p. 27°.

Mononitrotartaric esters, $RO_2C{\cdot}CH(ONO_2)CH(OH){\cdot}CO_2R$; *dimethyl ester*, m.p. 97° ; *diethyl ester*, m.p. 47°. Both the series of compounds are formed together when tartaric esters are treated with nitric and sulphuric acids (C. 1903, I. 627 : Ber. **36**, 778).

(3) *lævo*-**Tartaric acid,** m.p. 167–170°, is very similar to the *dextro*-variety, and only differs from it in rotating the ray of polarized light to the left. Their salts are very similar, and usually isomorphous, but those of the *lævo*-acid exhibit opposite hemihedral faces.

The dimethyl ester has the same melting and boiling points as the dimethyl ester of *d*-tartaric acid (see above) ; *cf.* also racemic acid esters (p. 656). In the description of racemic acid the method by which *l*-tartaric acid could be obtained from it was exhaustively considered (p. 656). In concentrated solution it combines with *d*-tartaric acid and yields racemic acid.

(4) *meso***Tartaric acid,** *inactive tartaric acid,* anti*tartaric acid,* is obtained by oxidizing parasorbic acid or erythritol with nitric acid : together with racemic acid by the action of silver oxide on dibromosuccinic acid or from maleic acid or phenol by oxidation with permanganate (Ber. **24**, 1753). It is prepared by heating *d*-tartaric acid with water at 165° for two days, or by the oxidation of maleic acid.

It contains one molecule of water of crystallization.

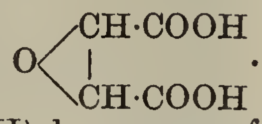
Salts.—Calcium salt, $C_4H_4O_6Ca + 3H_2O$ (Ann. **226**, 198). *Barium salt.* $C_4H_4O_6Ba + H_2O$ (Ann. **292**, 315).

Methyl ester, m.p. 111°, *ethyl ester,* m.p. 54°, b.p. 156°/14 mm. (Ber. **21**, 517). The *nitrile,* CN·CHOH·CHOH·CN, m.p. 131° (decomp.) is obtained from hydrogen cyanide and glyoxal in alcoholic solution. *Nitrile* of *diacetyl derivative,* m.p. 76° (Ber. **76**, R. 749).

Chloromalic acids, *α-chloro-β-hydroxysuccinic acids,* HOCO·CHCl·CHOH·COOH. (I) The *dl-meso* form, m.p. 143°, is obtained from maleic acid and hypochlorous acid and gives with alkalis *trans*-fumarylglycidic acid (see below) (Ann. **348**, 299 : Ber. **58**, 919 : **61**, 490), and on heating with water a mixture of racemic acid and *meso*-tartaric acid. (II) The *dl-racemic* form, m.p. 153°, is formed together with the (I) acid from fumaric acid and hypochlorous acid or by the addition of hydrochloric acid to *cis*-ethylene oxide dicarboxylic acid (below). Removal of hydrochloric acid by the action of concentrated alkalis yields the *cis*-ethylene oxide dicarboxylic acid and heating with water yields quantitatively *meso*tartaric acid (Ber. **58**, 919). *Bromomalic acid,* m.p. 134°.

The acids thus formed are optically inactive, but by the action of phosphorus pentachloride or tribromide on tartaric esters, *l*-chloro- or *l*-bromo- malic esters are formed, which on reduction yield malic esters (Ber. **28**, 1291 : Ann. **348**, 273 : Ber. **55**, 1339).

Ethylene oxide dicarboxylic acid, *fumarylglycidic acid.*



$O\left\langle\begin{array}{l}CH\cdot COOH\\ |\\ CH\cdot COOH\end{array}\right.$.

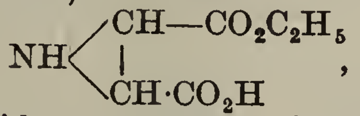
—The *cis*-acid, m.p. 149°, is obtained from chloromalic acid (II) by means of alkali, and on hydrolysis with water yields solely racemic acid : addition of HCl yields chloromalic acid (II). The *trans*-acid, *dl*-form, m.p. 209°, is obtained from chloromalic acid (I) with alkalis. It can be resolved by means of morphine. *d*-Form, $[\alpha]_D + 34{\cdot}8°$ (Ber. **58**, 928). The *dl-trans*-acid yields on heating with water a mixture of racemic and *meso*tartaric acids.

Diaminosuccinic acid, $COOH\cdot CH(NH_2)\cdot CH(NH_2)\cdot COOH$, is obtained by the reduction of the diphenylhydrazone of dihydroxytartaric acid by sodium amalgam. (Preparation, Ber. **58**, 1429.) The less soluble acid is the *meso*-form, the more soluble the *racemic.* (Resolution with morphine, Ber. **58**, 1429.) *Diethyl ester,* b.p. 160–165°/15 mm. *Diacetamidosuccinic acid diethyl ester,* m.p. 180° (Ber. **38**, 1589).

Hydroxyaminosuccinic acid, *hydroxyaspartic acid.* $COOH\cdot CH(NH_2)\cdot CH(OH)\cdot COOH$.—A mixture of the stereoisomeric forms of this acid is obtained by the action of one molecule of nitrous acid on diaminosuccinic acid, m.p. 314–318° (C. 1905, I. 1090 : Ann. **348**, 307). *Preparation* of the various hydroxyaspartic acids from chloromalic acid, J. Biol. Chem. **48**, 273. *Hydroxyasparagines,* $COOH\cdot CH(NH_2)\cdot CH(OH)\cdot CONH_2$ and $CONH_2\cdot CH(NH_2)\cdot CH(OH)\cdot COOH$, see Biochem. J. **24**, 945.

Dianilinosuccinic ester, $CO_2C_2H_5\cdot CH(NHC_6H_5)CH(NHC_6H_5)\cdot CO_2C_2H_5$, m.p. 149°, is obtained from dibromo- and *iso*dibromo-succinic ester and alcoholic aniline heated to 100° (Ber. **27**, 1604).

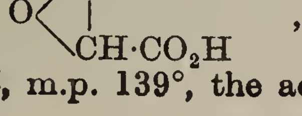
Iminosuccinic monoethyl ester,



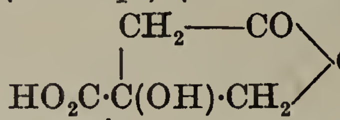
$NH\left\langle\begin{array}{l}CH{-}CO_2C_2H_5\\ |\\ CH\cdot CO_2H\end{array}\right.$, m.p. 98°, is prepared from iminosuccinic monoester amide, a product of the reaction of alcoholic ammonia and dibromosuccinic ester (Ber. **25**, 646).

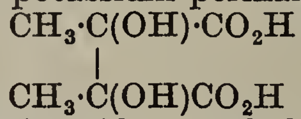
Azinsuccinic ester, $(CO_2C_2H_5)_2C_2H_2\cdot N_2\cdot C_2H_2(CO_2C_2H_5)$, is obtained from diazoacetic ester ; an isomeric ester is obtained from diazosuccinic ester (Ber. **29**, 763).

Oxycitraconic acid,



$O\left\langle\begin{array}{l}C(CH_3)\cdot CO_2H\\ |\\ CH\cdot CO_2H\end{array}\right.$, decomposes at 162°. It is formed when *α-chlorocitramalic acid,* m.p. 139°, the addition product of HClO and citraconic acid, is treated with alkali hydroxide. Hydrochloric acid changes it to *β-chlorocitramalic acid,* m.p. 162° (decomp.) (Ann. **253**, 87).

Hydroxyparaconic acid,  $\begin{array}{l} CH_2\text{——}CO\diagdown \\ \quad | \qquad\qquad\quad >O \\ HO_2C\cdot C(OH)\cdot CH_2\diagup \end{array}$ m.p. 104°, is prepared from itaconic acid (p. 571) and potassium permanganate.

Dimethylracemic acid,  $\begin{array}{l} CH_3\cdot C(OH)\cdot CO_2H \\ \quad | \\ CH_3\cdot C(OH)CO_2H \end{array} + H_2O$, m.p. 178° (decomp.), is formed (1) from pyroracemic acid (p. 462) by reduction (Ber. **25**, 397), and (2) from diacetyl (p. 402) by the action of HCN and hydrochloric acid (Ber. **22**, R. 137).

C. Glutaric Acid Derivatives

αβ-Dihydroxyglutaric acid, $HO_2C\cdot CH(OH)CH(OH)CH_2\cdot CO_2H$, m.p. 158°, is formed from the bromine addition product of glutaconic acid, or from the latter by permanganate. An optically active form of this acid has been obtained by the breakdown of metasaccharopentose (p. 676) (Ber. **38**, 3625).

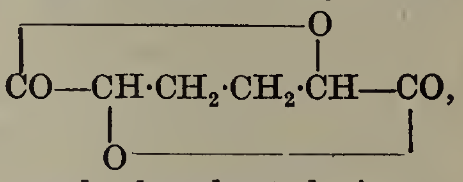
α-Amino-β-hydroxyglutaric acid, $COOH\cdot CH(NH_2)\cdot CH(OH)\cdot CH_2\cdot COOH$, is described on p. 614.

αγ-Dihydroxyglutaric acid, $HO_2C\cdot CH(OH)CH_2CH(OH)CO_2H$, m.p. 120°; *lactone acid,* m.p. 165°, is formed from αγ-dihydroxypropane-ααγ-tricarboxylic acid (the oxidation product of *iso*saccharin, p. 676) by loss of CO_2 (Ber. **18**, 2576; **38**, 3624).

αγ-Dihydroxy-αγ-dimethylglutaric acid, $HOCO\cdot CMe(OH)\cdot CH_2\cdot CMe(OH)\cdot COOH$, exists in two modifications, both of which are prepared from acetylacetone and hydrocyanic acid (Ber. **24**, 4006: **25**, 3221). The one, m.p. 98°, is obtained in enantiomorphous crystals from ether; the other readily passes into the *lactonic acid,* m.p. 90°, which, when heated, forms a *dilactone,* m.p. 105°, b.p. 235°.

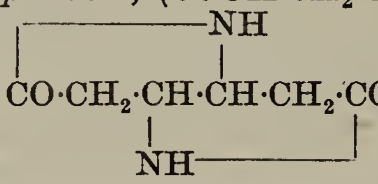
αβ-Dihydroxy-γγ-dimethylglutaric lactonic acid (p. 624); *αγ-dihydroxy-ββ-dimethylglutaric acid,* $(CH_3)_2C[CH(OH)CO_2H]_2$; lactonic acid, m.p. 146° (C. 1901, II. 109); *αγ-dihydroxy-* and *βγ-trimethylglutaric acid* (Ber. **28**, 2940).

D. Derivatives of Adipic Acid and Higher Homologues

αα′-Dihydroxyadipic acid, $HO_2C\cdot CH(OH)CH_2CH_2CH(OH)CO_2H$, exists in two forms which are produced from the corresponding *αα′-dibromoadipic acids,* m.pp. 139° and 193°, which occur together after the bromination of adipic acid chloride (C. 1908, I. 2021). The *racemic form,* m.p. 146°, is resolved by means of cinchonidine, and when heated yields a *dilactone,*  $\begin{array}{l} \overline{\;|\qquad\qquad\qquad\qquad\quad O} \\ CO\text{—}CH\cdot CH_2\cdot CH_2\cdot CH\text{—}CO \\ \qquad\; |\qquad\qquad\qquad\qquad\quad | \\ \qquad\; O\text{—————————}\! \end{array}$, m.p. 134°; *meso-form,* m.p. 173°, is not resolvable, and when heated gives a lactone lactide.

αα′-Diaminoadipic acid, $(\text{—}CH_2CH(NH_2)CO_2H)_2$, decomposes at 275°, is prepared by decomposition of ethylene bis-phthalimidomalonic ester, a product of reaction of ethylene bromide and sodium phthalimidomalonic ester. Similarly, *αα′-diaminopimelic acid* is formed from trimethylene bis-phthalimidomalonic ester (C. 1908, II. 682).

ββ′-Diaminoadipic acid, $(COOH\cdot CH_2\cdot CH(NH_2)\text{—})_2$, $+ H_2O$.

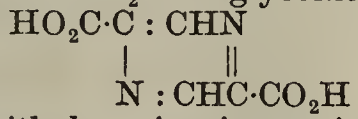
The dilactam,  $\begin{array}{l} \overline{\;|\qquad\qquad\qquad NH} \\ CO\cdot CH_2\cdot CH\cdot CH\cdot CH_2\cdot CO \\ \qquad\qquad |\qquad\qquad\quad | \\ \qquad\qquad NH\text{————}\! \end{array}$, m.p. 275°, is formed by heating muconic acid or muconic amide (p. 577) with ammonia to 135–150°; also by reduction of dicyanodimalonic ester, $(RO_2C)_2\cdot CHC(NH)\cdot C(NH)CH(CO_2R)$, (p. 720), and subsequent hydrolysis and abstraction of CO_2 (Ber. **36**, 172).

αα′-Diaminosuberic acid, αα′-diaminosebacic acid, αα′-diaminoazelaic acid, are prepared from the corresponding dicarboxylic acid by bromination and reaction with two molecules of NH_3. When heated they break down into CO_2 and alkylene diamines (p. 382) (C. 1905, II. 462 : 1906, II. 764). *Dihydroxydimethyladipic acids* are formed from acetonylacetone and hydrocyanic acid (Ber. **29**, 819).

Cineolic acid, $C_{10}H_{16}O_5$, is the anhydride of α-hydroxy*iso*propyl-α-methyl-α-hydroxyadipic acid, comparable to the alkylene oxides (see Cineol, Vol. II).

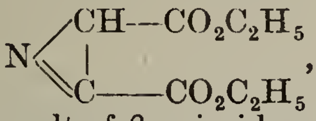
Dihydroxysuberic acid and *dihydroxysebacic acid* ; see Adipic dialdehyde and Suberic dialdehydes (p. 400) (C. 1905, II. 462 : 1907, II. 1236).

(ii) DIHYDROXYOLEFINECARBOXYLIC ACIDS

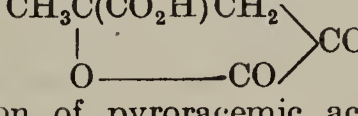
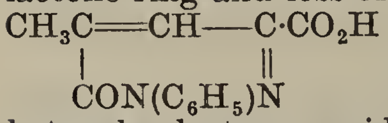
Dihydroxymaleic acid, $HO_2C\cdot C(OH):C(OH)\cdot CO_2H + 2H_2O$, may perhaps be looked on as being oxalohydroxyacetic acid, $HO_2CCO\cdot CH(OH)CO_2H$ (Ann. **357**, 291). It is formed when tartaric acid is oxidized with hydrogen peroxide in presence of small quantities of ferrous salts in sunlight. When warmed with HBr in glacial acetic acid it is converted into an isomeric body, probably dihydroxyfumaric acid. When heated with water it decomposes into $2CO_2$ and glycollic aldehyde ; ammonia produces pyrazinedicarboxylic acid,  $\begin{array}{l} HO_2C\cdot C:CHN \\ \quad\; | \qquad \| \\ \quad N:CHC\cdot CO_2H \end{array}$ Oxidation of the sodium salt of dihydroxymaleic acid with bromine in acetic acid gives rise to sodium dihydroxytartrate (p. 662) ; whilst oxidation with ferric salts produces glyoxyl carboxylic acid (p. 600) (C. 1905, II. 456). *Diacetyldihydroxymaleic acid*, m.p. 98°. See also *dichloro-* and *dibromo-maleic acids*, and their decomposition products (p. 569) (Ber. **38**, 258).

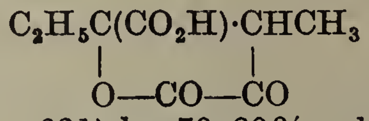
12. HYDROXYKETODICARBOXYLIC ACIDS

Ethoxyoxaloacetic ester, $C_2H_5O_2C\cdot COCH(OC_2H_5)CO_2C_2H_5$, b.p. 155°/11 mm., is prepared from oxalic ester and ethyl glycollic ester. When distilled under ordinary pressure it gives ethoxymalonic ester (Ber. **31**, 552). See also Dihydroxymaleic acid (above).

Nitrilosuccinic dimethyl ester,  $N\begin{array}{l} \diagup CH\text{—}CO_2C_2H_5 \\ \quad | \\ \diagdown\!\!\diagdown C\text{——}CO_2C_2H_5 \end{array}$, b.p. 154°/40 mm., is produced by the reaction of the silver salt of β-oximidosuccinic ester (p. 621) and iodoethane and subsequent distillation (Ber. **23**, R. 561 : **24**, 2289).

Glycolylmalonic acid ; *γ-hydroxyacetoacetic-α-carboxylic acid*, $HOCH_2COCH(CO_2H)_2$, is a hypothetical acid, from which is derived *tetronic-α-carboxylic acid*, $\overline{OCH_2COCH(CO_2H)CO}$; *methyl ester*, m.p. 172° (decomp.) ; *ethyl ester*, m.p. 125°. The substances are prepared from sodium malonic ester and acetyl glycollic chloride or chloroacetyl chloride. The desmotropic *aci*-forms, $\overline{OCH_2C(OH):C(CO_2R)CO}$, are strong acids like tetronic acid itself (p. 599) into which they pass on hydrolysis and loss of CO_2. Sodium cyanoacetic ester and chloroacetyl chloride produce *chloroacetylcyanoacetic esters*, $ClCH_2COCH(CN)CO_2R$; *methyl ester*, m.p. 73° ; *ethyl ester*, 43°. The silver salt and iodoethane yield the O-*ethyl ether* of the *aci*-form, $ClCH_2C(OC_2H_5):C(CN)CO_2C_2H_5$, m.p. 94°, which with ammonia gives the *amino*-compound, $ClCH_2\cdot C(NH_2):C(CN)CO_2CH_5$, m.p. 129°. The sodium salt of chloroacetyl cyanoacetic ester, however, reacting with ammonia forms a lactone—*cyanoketopyrrolidone*, $\overline{NHCH_2COCH(CN)CO}$, m.p. 221° (decomp.) (Ber. **41**, 2399). Homologous with the tetronic carboxylic esters is *carbotetrinic ester*, $\overline{OCH_2COCH(CH_2CO_2C_2H_5)CO}$, m.p. 96°, which results from distillation of bromoacetosuccinic ester.

α-Keto-γ-valerolactone-γ-carboxylic acid,  $\left.\begin{array}{l} CH_3C(CO_2H)CH_2 \\ | \\ O\text{————}CO \end{array}\right\rangle CO$, m.p. 117°, results from the spontaneous decomposition of pyroracemic acid (p. 462), or more quickly under the influence of hydrochloric acid. It reacts also in the tautomeric enol-form, yielding a *phenylhydrazone,* which, on cleavage of the lactone ring and loss of water, passes into *phenylmethylpyridazonecarboxylic acid,* (Vol. III).  Alcoholic hydrochloric acid converts the ketovalerolactone acid into *γ-methylketoglutaconic ester,* $CH_3C(CO_2C_2H_5):CH\cdot COCO_2C_2H_5$, b.p. 183°/28 mm., whilst hot strong hydrochloric acid produces pyrotartaric acid (p. 548) (Ann. **317**, 1 : **319**, 121 : C. 1902, II. 508 : 1904, II. 193).



α-Keto-β-methyl-γ-caprolactone-γ-carboxylic acid, , m.p. 128°, is produced from α-methyloxaloacetic ester (p. 621) by 70–80% sulphuric acid (Ber. **35**, 1626).

13. DIKETONEDICARBOXYLIC ACIDS

Dihydroxytartaric acid, $HOCO\cdot C(OH)_2\cdot C(OH)_2\cdot COOH$, m.p. 98° (decomp.), is obtained (1) when protocatechuic acid, pyrocatechin, or guaiacol (Vol. II), in ethereal solution, is acted on with nitrous acid ; (2) by oxidation of dihydroxymaleic acid ; and (3) by spontaneous decomposition of nitrotartaric acid (see Ann. **302**, 291, footnote : J.A.C.S. **43**, 577).

It was formerly regarded as carboxytartronic acid, $C(OH)(CO_2H)_3$. Its formation from the benzene derivatives was cited as proof for the assumption that in benzene one carbon atom is combined with three other carbon atoms. However, Kekulé removed the basis from this assumption when he showed that the body supposed to be carboxytartronic acid could also be made from nitrotartaric acid by the action of an alcoholic solution of nitrous acid, and then by reduction be converted into racemic and mesotartaric acids. He therefore named it dihydroxytartaric acid, for it sustains the same relation to tartaric acid that glyoxylic acid bears to glycollic acid, and mesoxalic acid to tartronic acid (Ann. **221**, 230). On reduction by suitable methods, dihydroxytartaric acid yields dihydroxymaleic acid (p. 661 : C. 1898, I. 31).

By the action of alkalis according to the concentration, dihydroxytartaric acid either undergoes a simple decomposition into oxalic and glyoxylic acids (Equation I) or yields tartronic acid by loss of carbon dioxide from the product of a benzilic acid transformation (J.A.C.S. **43**, 2091) (Equation II : see also Vol. II).

$$\text{I. } COOH\cdot CO\cdot CO\cdot COOH \longrightarrow (COOH)_2 + O:CH\cdot COOH \text{ (C. 1922, I. 1068).}$$

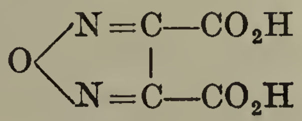
$$\text{II. } COOH\cdot CO\cdot CO\cdot COOH \longrightarrow [COOH\cdot C(OH)(COOH)_2] \longrightarrow COOH\cdot CHOH\cdot COOH + CO_2.$$

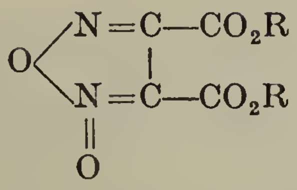
Glyoxal (p. 398) is obtained by the action of sodium bisulphite on the sodium salt of dihydroxytartaric acid.

The *sodium salt,* $C_4H_4O_8Na_2 + 2H_2O$, is a very sparingly soluble crystalline powder, which is used for the isolation of the acid, and also for the quantitative estimation of sodium (C. 1898, I. 688). Other salts, see C. 1898, II. 276 : 1905, II. 397.

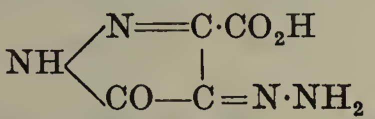
Esters.—The esters of the acid, $COOH\cdot C(OH)_2\cdot C(OH)_2\cdot COOH$, are not known. The *ester,* $C_2H_5OCO\cdot C(OH)_2\cdot CO\cdot COOC_2H_5$, m.p. 116–118°, colourless crystals, is obtained by the addition of water to *ethyl diketosuccinate,* $C_2H_5OCO\cdot CO\cdot CO\cdot COOC_2H_5$, b.p. 233°, b.p. 116°/13 mm., D_{20} 1·1896, and reverts to the latter when distilled under diminished pressure. The diketo ester, which is a thick liquid with a yellow colour (*cf.* α-diketones, p. 401), is obtained by the action of hydrochloric acid on sodium dihydroxytartrate suspended in alcohol. When boiled under a reflux condenser, CO is lost and mesoxalic ester (p. 617) and oxalic ester are formed.

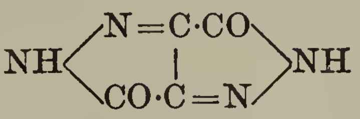
Oximes.—*Dioximinosuccinic acid,* $HO_2C\cdot C(NOH)C(NOH)\cdot CO_2H$, and its *esters* have been obtained in different stereomeric forms (C. 1908, I. 1042, etc.). The *dioxime anhydride, furazandicarboxylic acid* (1) is prepared by oxidation of dimethyl furazan (*cf.* p. 408) ; the *furoxan* derivative (2) from *iso*nitrosoacetic ester (p. 460) or *iso*nitrosoacetoacetic ester (p. 602) and nitric acid. It is an easily decomposable oil (Ber. **28**, 1213).

(1) 

(2) 

Hydrazones.—Hydrazopyrazoloncearboxylic acid (1) and *pyrazolonopyrazolone* (2) may be taken as being the *lactazam* and *dilactazam* (*cf.* p. 461) of the mono- and dihydrazone of diketosuccinic acid (see Vol. II).

(1) 

(2) 

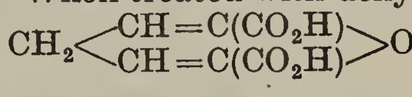
Diketosuccinic ester monophenylhydrazone, $C_6H_5NH{\cdot}N:C(CO_2C_2H_5){\cdot}CO{\cdot}CO_2{\cdot}C_2H_5$, m.p. 73°, is formed from oxaloacetic ester (p. 620) and diazobenzene. It is converted into a *stereomeric hydrazone*, m.p. 127°, by sodium alcoholate (C. 1904, I. 580). The *osazone* of diketosuccinic acid readily passes into the *lactazam, phenylhydrazophenylpyrazolonecarboxylic acid*, $C_6H_5N{\cdot}N:C(CO_2H)C(NNHC_6H_5){\cdot}CO$, the basis of the dye *tartrazine*. *Diketosuccinic diethyl ester osazone* $[C_6H_5NHN:C(CO_2C_2H_5)]_2$ is known in *three* modifications, α-, m.p. 121°; β-, m.p. 137°; γ-, m.p. 175°. The α-form gradually passes spontaneously into the β-substance, a change which is accelerated by iodine or sulphur dioxide. All three forms are readily converted into pyrazolone compounds.

Oxalodiacetic acid, *ketipic acid*, $HO_2CCH_2{\cdot}COCO{\cdot}CH_2CO_2H$, is precipitated from the ester by concentrated hydrochloric acid, as a white insoluble powder. Heat decomposes it into $2CO_2$ and diacetyl. The *ester*, $C_2H_5O_2CCH_2{\cdot}COCO{\cdot}CH_2{\cdot}CO_2C_2H_5$, m.p. 77°, is prepared, similarly to oxaloacetic ester (p. 620) from a mixture of oxalic ester and two molecules of acetic ester by the action of sodium (Ber. **20**, 591); also, from oxalic ester and chloroacetic ester and zinc (Ber. **20**, 202). An alcoholic solution of the ester is given an intense red coloration by ferric chloride. Chlorine and bromine produce *tetrachloro-* and *tetrabromo-*derivatives. *Tetrachlorodiketoadipic ester* is also obtained by the action of chlorine on dihydroxyquinone dicarboxylic ester (Ber. **20**, 3183). The osazone of oxalodiacetic ester can be converted into *di-1-phenyl-3:3-bis-pyrazolone* (Vol. II) (Ber. **28**, 68).

α-Oxaloacetoacetic ester, $HO_2CCO{\cdot}CH(COCH_3)CO_2H$, is not known, but the derivative, *α-cyaniminoacetoacetic ester*, $NCC(NH)CH(COCH_3)CO_2C_2H_5$, m.p. 122°, has been prepared from cyanogen and acetoacetic ester by the action of sodium ethoxide (*cf.* p. 473). Acids or secondary amines convert it into two isomeric forms, m.pp. 178° and 211°, of the various possible desmotropic modifications of the enol type, and with absorption of water into *α-acetyl-β-iminosuccinamic ester*, and finally into *α-acetyl-β-iminosuccinimide* (Ann. **332**, 104).

γ-Oxalo-α-dimethylacetoacetic ester, $C_2H_5O_2C{\cdot}CO{\cdot}CH_2COC(CH_3)_2CO_2C_2H_5$, is obtained by condensing oxalic ester and α-dimethylacetoacetic ester. When distilled under ordinary pressure there is a partial loss of CO. The *acid*, m.p. 180° with decomposition into CO_2 and $(CH_3)_2CHCO{\cdot}CH_2COCO_2H$. *Oxalódiethylacetoacetic ester*, $C_2H_5O_2C{\cdot}CO{\cdot}CH_2C(C_2H_5)_2CO_2C_2H_5$, b.p. 275–285° with decomposition into CO and α-diethylacetonedicarboxylic ester (p. 624). These esters are in general similar to oxaloacetic ester (Ber. **33**, 3432).

δ-Oxalolævulinic acid, αγ-diketopimelic acid, $HO_2C{\cdot}CO{\cdot}CH_3COCH_2CH_2CO_2H$, m.p. 100–125°, is obtained from its *ethyl ester*, m.p. 19°, the condensation product of oxalic ester and lævulinic ester by warming the two esters with sulphuric acid. When heated the acid breaks down into CO_2, CO, and lævulinic acid. Reduction produces pimelic acid (Ber. **31**, 622).

αε-Diketopimelic acid, $CH_2(CH_2COCO_2H)_2$, m.p. 127°, is obtained from methylene bis-oxaloacetic ester by hydrolysis and loss of CO_2. When treated with dehydrating agents there is formed *pyrandicarboxylic acid*,  $CH_2{<}{\begin{matrix}CH=C(CO_2H)\\CH=C(CO_2H)\end{matrix}}{>}O$, decomposes at 250° (Vol. III) (C. 1904, II. 602).

sym.-*Diacetyl-* or *Diacetosuccinic acid*, $C_8H_{10}O_6$; *ethyl ester* is formed by electrolysis or the action of iodine on sodium acetoacetic ester (Ann. **201**, 144 : Ber. **28**, R. 452):

$$\begin{array}{l} CH_3CO{\cdot}CHNa{\cdot}CO_2R \\ CH_3CO{\cdot}CHNa{\cdot}CO_2R \end{array} + I_2 = \begin{array}{l} CH_3CO{\cdot}CH{\cdot}CO_2R \\ \qquad\quad | \\ CH_3CO{\cdot}CH{\cdot}CO_2R \end{array} + 2\,NaI.$$

Theory demands the existence of 13 isomeric forms of this body—two optically active, and two optically inactive keto-forms, three cis-trans isomers of the double enol-form, and four optically active and two racemic mixed keto-enol-forms. Of the seven optically inactive modifications, five are known : β- and γ-*keto*-forms, m.pp. 90° and 30° : *dienol* form, α-ester, m.p. 45° : *ketoenol* forms, $\alpha_1\beta$-ester, liquid, $\alpha_2\beta$-ester, m.p. 20° (Ber. **55**, 232). Equilibrium between the various forms is reached via the $\alpha_1\beta$-form (Ber. **55**, 2257). When heated or acted on by acids, diacetosuccinic ester is converted into carbopyrotritaric ester (a derivative of furan) ; ammonia and the amines produce pyrrole derivatives—a reaction which serves to identify the substance (Ber. **19**, 46). *Phenylhydrazine* reacts as it does with acetoacetic ester, forming a bis-pyrazolone derivative (Ann. **238**, 168).

When boiled with potash solution the ester undergoes the ketonic change into CO_2 and acetonylacetone (p. 405).

as.-*Diacetosuccinic ester*, $(CH_3CO)_2C(CO_2C_2H_5)CH_2CO_2C_2H_5$, b.p. 275°, is formed from sodium acetosuccinic ester and acetyl chloride (J. pr. Chem. [2] **65**, 532).

αβ-Diacetoglutaric acid, $HO{\cdot}CO{\cdot}CH(COCH_3){\cdot}CH(COCH)_3{\cdot}CH_2{\cdot}COOH$. Its *diethyl ester* is obtained from sodium acetoacetic ester and β-bromolævulinic ester (p. 479). Being a γ-diketone compound, it unites with ammonia and forms a pyrrole derivative (Ber. **19**, 47).

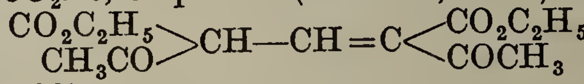
αγ-Diacetoglutaric ester, $EtO \cdot CO \cdot CH(COCH_3) \cdot CH_2 \cdot CH(COCH_3)COOEt$, is formed from formaldehyde and acetoacetic ester in the presence of small quantities of a primary or secondary amine (*Knoevenagel*, Ann. **288**, 321 : Ber. **31**, 1388). It passes readily into a tetrahydrobenzene derivative. The β-alkyl-αγ-diacetoglutaric esters prepared from the homologous aldehydes behave in a similar manner.

αδ-Diacetoadipic acid, $(—CH_2CH(COCH_3){\cdot}CO_2H)_2$. Ethylene bromide acting on two molecules of sodium acetoacetic ester, forms its diethyl ester. Phenylhydrazine converts it into a bis-pyrazolone derivative (Ber. **19**, 2045).

Diacetodimethylpimelic acid (Ber. **24**, R. 729).

Dilævulinic acid, [4 : 7-Decane dione diacid,] $(—CH_2COCH_2CH_2CO_2H)_2$, results when alcoholic hydrochloric acid acts on δ-furfural lævulinic acid (Ann. **294**, 167).

Iodine converts disodium diacetosuccinic ester into *diacetofumaric ester*, $EtO{\cdot}CO{\cdot}C(COCH_3) : C(COCH_3){\cdot}CO_2Et$, m.p. 96° (Ber. **30**, 1991).

Methenylbis-acetoacetic ester, 

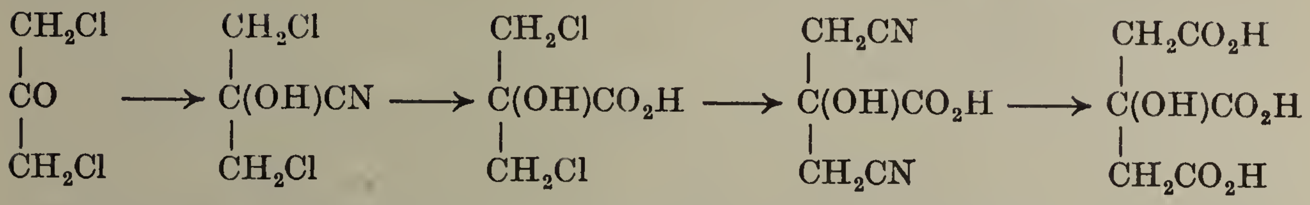
$$\begin{array}{r} CO_2C_2H_5 \\ CH_3CO \end{array}\!\!>CH—CH=C<\!\!\begin{array}{l} CO_2C_2H_5 \\ COCH_3 \end{array}$$

—see ethoxymethyleneacetoacetic ester (p. 601).

14. HYDROXYTRICARBOXYLIC ACIDS

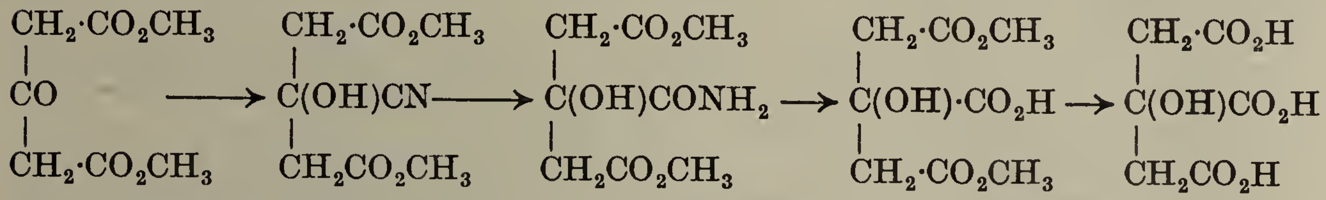
Citric acid, *hydroxytricarballylic acid* (*Acidum citricum*), $CO_2H{\cdot}CH_2{\cdot}C(OH)(CO_2H){\cdot}CH_2CO_2H + H_2O$, m.p. (anhydrous) 153°, occurs free in lemons, in currants, in cranberries, in beets, and in other acid fruits. It is obtained on a commercial scale from lemon juice, and by the action of certain ferments, such as *Citromycetes pfefferianus* and *glaber* (Ber. **26**, R. 696 : **27**, R. 78, 448).

The acid can be prepared synthetically from *sym.*-dichloroacetone ; this is accomplished by first acting on the latter compound with hydrocyanic acid and hydrochloric acid, whereby dichlorohydroxy*iso*butyric acid is formed, which is then treated with potassium cyanide producing a dicyanide, which is hydrolysed with hydrochloric acid :



$$\begin{array}{c}CH_2Cl\\|\\CO\\|\\CH_2Cl\end{array}\longrightarrow\begin{array}{c}CH_2Cl\\|\\C(OH)CN\\|\\CH_2Cl\end{array}\longrightarrow\begin{array}{c}CH_2Cl\\|\\C(OH)CO_2H\\|\\CH_2Cl\end{array}\longrightarrow\begin{array}{c}CH_2CN\\|\\C(OH)CO_2H\\|\\CH_2CN\end{array}\longrightarrow\begin{array}{c}CH_2CO_2H\\|\\C(OH)CO_2H\\|\\CH_2CO_2H\end{array}$$

Further, citric acid is formed from acetonedicarboxylic esters, $CO(CH_2{\cdot}CO_2R)_2$ (p. 623), by the action of HNC and hydrochloric acid : *sym.*-citric dimethyl ester amide and *sym.*-citric dimethyl ester (p. 666) are obtained as intermediate substances :

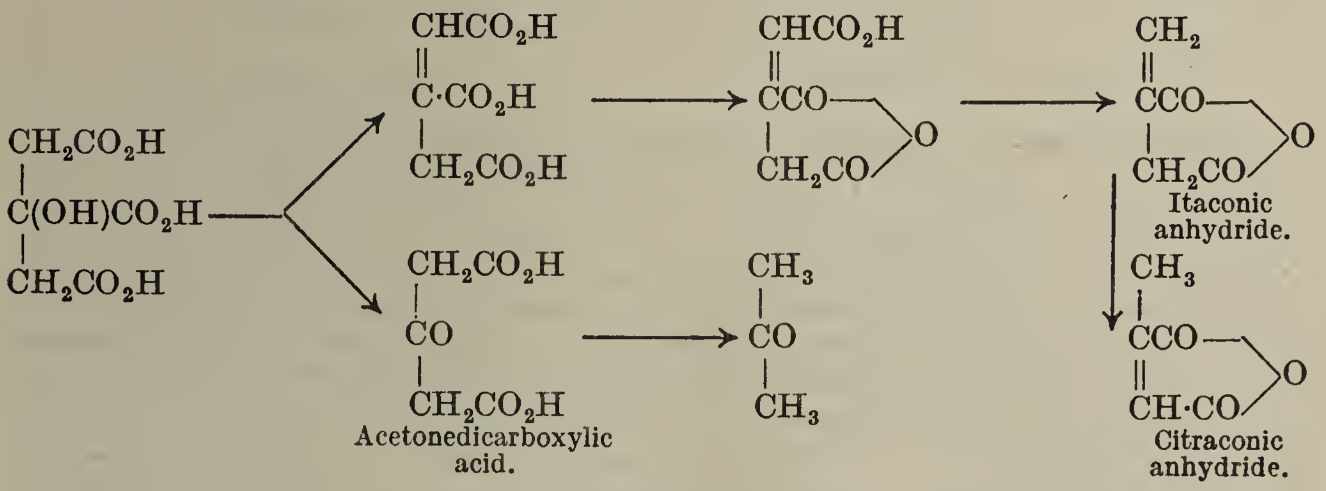


$$\begin{array}{c}CH_2{\cdot}CO_2CH_3\\|\\CO\\|\\CH_2{\cdot}CO_2CH_3\end{array}\longrightarrow\begin{array}{c}CH_2{\cdot}CO_2CH_3\\|\\C(OH)CN\\|\\CH_2CO_2CH_3\end{array}\longrightarrow\begin{array}{c}CH_2{\cdot}CO_2CH_3\\|\\C(OH)CONH_2\\|\\CH_2CO_2CH_3\end{array}\longrightarrow\begin{array}{c}CH_2{\cdot}CO_2CH_3\\|\\C(OH){\cdot}CO_2H\\|\\CH_2{\cdot}CO_2CH_3\end{array}\longrightarrow\begin{array}{c}CH_2{\cdot}CO_2H\\|\\C(OH)CO_2H\\|\\CH_2CO_2H\end{array}$$

Ethyl citrate is also obtained in small yield by the action of zinc on bromoacetic ester and oxaloacetic ester (C. 1897, I. 802).

Properties.—Citric acid crystallizes in large rhombic prisms, which dissolve in 4 parts of water at 20°, the anhydrous acid crystallizes mostly anhydrous from its solutions (Ber. **36**, 3599). It readily dissolves in alcohol and with difficulty in ether. The aqueous solution is not precipitated by milk of lime when cold, but on boiling the tertiary calcium salt separates, which is insoluble, even in potassium hydroxide solution (see Tartaric acid).

When heated to 175° citric acid decomposes into aconitic acid (p. 648). Rapidly heated to a higher temperature aconitic acid breaks down into water and its anhydride acid, which changes to CO_2 and itaconic anhydride, and the latter in part to citraconic anhydride (Ber. **13**, 1541). Another portion of the citric acid loses water and CO_2, becoming converted thereby into acetone dicarboxylic acid, which immediately splits into $2CO_2$ and acetone :



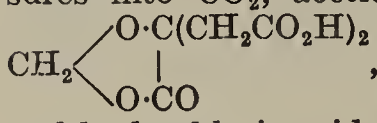
It breaks up into acetic and oxalic acids when fused with potassium hydroxide, and by oxidation with nitric acid. Acetonedicarboxylic acid (p. 623) is produced when citric acid is digested with concentrated sulphuric acid, and when oxidized with permanganate (C. 1900, I. 328).

Salts.—Being a tribasic acid it forms three series of salts, and also two different mono- and two different di-alkali salts (Ber. **26**, R. 687).

The *calcium salt*, $(C_6H_5O_7)_2Ca_3 + 4H_2O$, is precipitated on boiling.

Esters.—*Trimethyl ester*, m.p. 79°, b.p. 176°/16 mm. ; *dimethyl ester*, $CH_2(CO_2CH_3)C(OH)(CO_2H)CH_2CO_2CH_3$, m.p. 126°, is formed by partial esterification of the acid. It crystallizes with 1 molecule of water and is difficultly soluble in cold water (Ber. **35**, 2085).

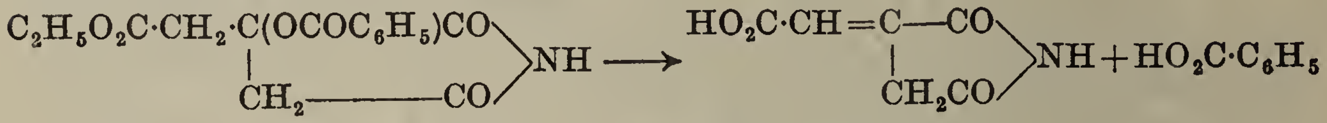
Acetocitric trimethyl ester, b.p. 171°/15 mm., is decomposed by distillation at ordinary pressures into acetic acid and aconitic ester (Ber. **18**, 1954). sym.-*Acetocitric dimethyl ester*, m.p. 75° ; *amide*, m.p. 109° (Ber. **38**, 3194). *Acetocitric anhydride*, m.p. 121° (Ber. **22**, 984), decomposes on distillation at ordinary pressures into CO_2, acetic acid, and citraconic anhydride. *Methylene citric acid*, , m.p. 208°, is prepared from citric acid, formaldehyde, and hydrochloric acid ; or from formaldehyde derivatives (C. 1902, I. 299, 738 : 1908, I. 1589).



$$CH_2\begin{array}{l}\diagup O\cdot C(CH_2CO_2H)_2\\ \quad |\\ \diagdown O\cdot CO\end{array}$$

Methyl ether : methoxytricarballylic acid, $(CH_3O)C(CO_2H)(CH_2CO_2H)_2$, m.p. 131° ; *trimethyl ester*, b.p. 165°/12 mm., is prepared from citric trimethyl ester, iodomethane, and silver oxide (Ann. **327**, 228).

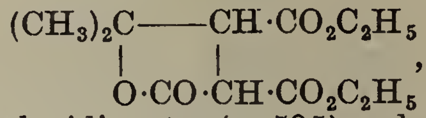
Citramide, $C_3H_4(OH)(CONH_2)_3$, when heated with hydrochloric or sulphuric acid, is condensed to *citrazinic acid* (sym.-*aconitimide acid, dihydroxypyridine carboxylic acid* (p. 648) (Ber. **17**, 2687 : **23**, 831 : **27**, R. 83). sym.-*Citric dimethyl ester amide*, $NH_2OC\cdot C(OH)(CH_2\cdot CO_2Me)_2$, m.p. 107°, is prepared from the *nitrile, acetonedicarboxylic ester cyanohydrin*, m.p. 53°, and reacts in concentrated sulphuric acid with sodium nitrite to form *sym.*-citric dimethyl ester (above). *Benzoylcitrimide ethyl ester*, m.p. 115°, is prepared from *citric diethyl ester amide*, m.p. 74°, and benzoyl chloride. It is decomposed in the cold by aqueous sodium hydroxide into benzoic acid and *as.*-aconitimido-acid (p. 648) which is isomeric with citrazinic acid (see above) (Ber. **38**, 3193) :



*iso***Citric acid**, $CO_2H\cdot CH(OH)\cdot CH(CO_2H)\cdot CH_2CO_2H$ (see Trichloromethyl paraconic acid, p. 612), readily passes into a *γ-lactone dicarboxylic acid* ; ester, b.p. 149°/14 mm., is formed by reduction of oxalosuccinic ester (Ann. **285**, 7).

α-Methyl*iso*citric acid, $CO_2H\cdot C(CH_3)(OH)\cdot CH(CO_2H)\cdot CH_2CO_2H$, is formed from acetosuccinic ester, hydrocyanic, and hydrochloric acids. When separated from its salts it immediately changes into *βγ-dicarboxy-γ-valerolactone*, which is also formed by oxidation of *iso*propylsuccinic acid, and from terebic acid by the oxidizing action of nitric acid. When heated it decomposes into H_2O, CO_2, and pyrocinchonic anhydride (Ber. **32**, 3861).

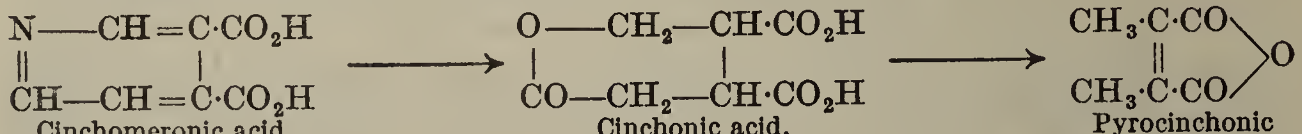
γ-Dimethylbutyrolactone-αβ-dicarboxylic ester, , m.p. 46°, b.p. 174°/12 mm., is prepared from *β*-methylglycidic ester (p. 595) and sodium malonic ester. When boiled with hydrochloric acid, it yields terebic acid (p. 612) (C. 1906, II. 421).



$$\begin{array}{ll}(CH_3)_2C & \!\!\!-\!\!\!-CH\cdot CO_2C_2H_5\\ \quad | & \quad |\\ O\cdot CO\cdot & CH\cdot CO_2C_2H_5\end{array}$$

αα-Dimethyl-γ-hydroxytricarballylic lactone acid (Ber. **30**, 1960), is formed from αα-dimethyl tricarballylic acid (see decomposition products of pinene (Vol. II).

Cinchonic acid, *δ-Valerolactone-βγ-dicarboxylic acid*, m.p. 168° (Ann. **234**, 85 : Ber. **25**, R. 904), is produced when sodium amalgam acts on cinchomeronic acid or 3 : 4-pyridinedicarboxylic acid. When heated to 168° it breaks down into CO_2 and pyrocinchonic anhydride (p. 574) :



Cinchomeronic acid. Cinchonic acid. Pyrocinchonic anhydride.

15. KETONETRICARBOXYLIC ACIDS

Carbethoxyoxaloacetic ester, oxalomalonic ester, $C_2H_5O_2C\cdot CO\cdot CH(CO_2C_2H_5)_2$, b.p. 220°/10 mm., is obtained from sodium malonic ester and ethyl oxalyl chloride (C. 1898, I. 440). Nitrogen derivatives of carboxy-oxaloacetic acid include *dicyanomalonic ester*, *β-cyano-β-imino*-iso*succinic ester*, $NC\cdot C(NH)CH(CO_2C_2H_5)_2$, m.p. 93°, which is prepared from cyanogen and malonic ester by means of sodium methoxide (p. 543). It can be hydrolysed to *dicyanomalonic mono-ester*, m.p. 238°, and *imido-oxalomalonic mono-ester*, m.p. 134° (decomp.), is reduced by sodium amalgam to *α-asparaginecarboxylic acid*, $NH_2COCH(NH_2)CH(CO_2H)_2$, m.p. 120° (decomp.) (Ann. **332**, 118). *α-Cyanooxaloacetic ester*, $C_2H_5O_2C\cdot COCH(CN)CO_2C_2H_5$, m.p. 96°, is formed from oxalic mono-ester chloride and sodium cyanoacetic ester. It is a strong acid (C. 1905, I. 1312).

Acetonetricarboxylic ester, $C_2H_5O_2C\cdot CH_2COCH(CO_2C_2H_5)_2$, is formed from malonic ester and sodium (p. 543). *Cyanoacetonedicarboxylic ester*, $C_2H_5O_2C\cdot CH_2COCH(CN)CO_2C_2H_5$, m.p. 44°, is prepared from sodium acetonedicarboxylic ester and cyanogen chloride. Double decomposition of its salts with alkyl iodides produces *O*-alkyl ethers of the unsaturated enol form (C. 1901, I. 883). *αγ-Dicyanoacetoacetic ester*, $NC\cdot CH_2CO\cdot CH(CN)CO_2C_2H_5$, m.p. 88°, is prepared from chloroacetylcyanoacetic ester (p. 661) and potassium cyanide (Ber. **41**, 2403).

Oxalosuccinic ester, $EtO\cdot CO\cdot CO\cdot CH(CO_2Et)\cdot CH_2(CO_2Et)$, b.p. 155°/17 mm., is obtained from oxalic and succinic esters and sodium ethoxide. Heat at ordinary pressure decomposes it into CO and ethenyl tricarboxylic ester (p. 646) (Ber. **27**, 797). Since it is a β-ketonic acid its alcoholic solution becomes coloured red with ferric chloride and forms a pyrazolone derivative with phenylhydrazine (Ber. **27**, 797 : Ann. **285**, 1). The sodium salt of the ester reacts with alkyl iodides, producing the *O*-ester of the enol modification. Hydrochloric acid decomposes the ester into CO_2 and α-ketoglutaric acid, $HO_2C\cdot CH_2CH_2CO\cdot CO_2H$ (*cf.* p. 623) (C. 1908, II. 768).

α-Acetotricarballylic ester, $CH_3CO\cdot CH(CO_2C_2H_5)CH(CO_2C_2H_5)CH_2(CO_2C_2H_5)$, b.p. 175°/9 mm., is formed from chlorosuccinic ester or fumaric ester and sodium acetoacetic ester (Ber. **23**, 3756 : C. 1899, I. 180).

β-Acetotricarballylic ester, $C_2H_5O_2CCH_2C(COCH_3)(CO_2C_2H_5)CH_2CO_2C_2H_5$, b.p. 190°/16 mm., is prepared from sodium acetosuccinic ester and chloroacetic ester ; also it results as a subsidiary product during the formation of acetosuccinic ester (Ann. **295**, 94). (See also α-Acetoglutaric acid, p. 624.)

Olefine Ketotricarboxylic Acids

α-Acetoaconitic ester, $EtO\cdot CO\cdot CH(COCH_3)\cdot C(CO_2Et) : CH\cdot CO_2Et$, is formed by the reaction of chlorofumaric ester, chloromaleic ester or acetylenedicarboxylic ester with sodium acetoacetic ester (C. 1900, II. 92).

16. TETRACARBOXYLIC ACIDS

A. PARAFFINTETRACARBOXYLIC ACIDS

I. All COOH-groups attached to same Carbon Atom

Methanetetracarboxylic acid, $C(COOH)_4$, is known in the form of its esters, which are obtained from the sodium derivatives of the corresponding methanetricarboxylic esters and chloroformic ester (Ann. **397**, 361). *Methyl ester*, m.p. 74°, b.p. 163°/12 mm. : *ethyl ester*, m.p. 13·5°, b.p. 173°/12 mm. By hydrolysis with sodium alcoholate, one carboxyl group is split off and sodiomethanetricarboxylic esters reproduced : acid hydrolysis produces malonic acid, and the action of ammonia yields malonamide and urethane.

II. COOH-groups attached to different Carbon Atoms

Formation.—(1) By the action of iodine on sodium malonic esters. (2*a*) From the sodium derivatives of malonic esters and alkylene dihalogenides or halogen malonic esters. (2*b*) From sodium tricarboxylic esters and halogen acetic esters. (3) By the addition of sodium malonic esters to the esters of unsaturated dicarboxylic acids, etc. Usually they are only known in the form of their esters.

sym.-*Ethanetetracarboxylic acid, dimalonic acid*, $(CO_2H)_2CH—CH(COOH)_2$, m.p. 168°, heated to higher temperatures yields succinic acid. It is obtained from its ester by means of sodium hydroxide (Ber. **25**, 1158). The *ethyl ester*, m.p. 76°, b.p. 305° (decomp.), is produced by electrolysis (Ber. **28**, R. 450), or by the action of chloromalonic ester or of iodine on sodium malonic ester; and by heating dioxalosuccinic ester (p. 720): potassium hydroxide hydrolyses it to ethanetricarboxylic acid with the elimination of CO_2 (p. 646). See Ber. **28**, 1722, for the *dihydrazide*.

Sodium ethoxide converts ethanetetracarboxylic ester into a disodium derivative, which yields tetrahydronaphthalenetetracarboxylic ester (Ber. **17**, 449) with *o*-xylylene bromide, $C_6H_4(CH_2Br)_2$.

Ethylethanetetracarboxylic ester, Ber. **17**, 2785.

Dimethylethanetetracarboxylic ester, Ber. **18**, 1202: **28**, R. 451.

Diethylethanetetracarboxylic ester, Ber. **21**, 2085: **28**, R. 452.

Alkylenedimalonic Acids.—Methylene-, ethylene,- and trimethylene-dimalonic acids are included in this class. Their ethyl esters are produced when methylene iodide, ethylene bromide, and trimethylene bromide act on sodium malonic esters; also, by the action of aliphatic aldehydes on malonic ester in the presence of diethylamine, piperidine, and similar bases. In the latter case, the corresponding aldehyde amines are formed as intermediate compounds, such as methanol piperidine, $CH_2(OH)(NC_5H_{10})$, or methylene bis-piperidine, $CH_2(NC_5H_{10})_2$, which react with malonic ester to form alkylidenedimalonic esters.

Methylenedimalonic ester, *dicarboxyglutaric ester*, *propane-$\alpha\alpha\gamma\gamma$-tetracarboxylic ester*, $CH_2[CH(CO_2C_2H_5)_2]_2$, b.p. 205°/18 mm.; *dimethyl ester*, m.p. 48°, is formed (1) from formaldehyde or methylene iodide (Ber. **22**, 3294: **27**, 2345: **31**, 738, 2585), and malonic ester; also (2) by reduction of β-propylenetetracarboxylic ester (Ber. **23**, R. 240). Ammonia produces the *tetramide*, $CH_2[CH(CONH_2)_2]_2$, m.p. 249°, which, when heated above its melting point, passes into the *diimide*, $CH_2[CH(CO_2)NH]_2$ (J. pr. Chem. [2] **66**, 1). Sodium alcoholate and iodo-alkyls produce methylenedialkylmalonic esters, from which $\alpha\alpha'$-dialkylglutaric acids can be obtained by decomposition.

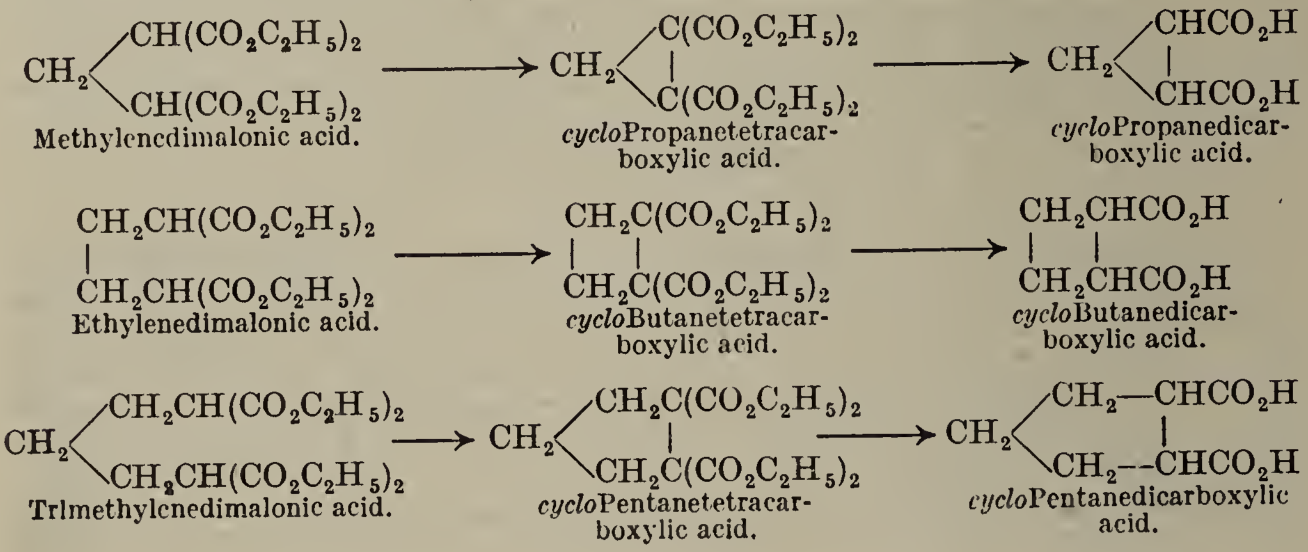
Ethylidenedimalonic ester, $CH_3{\cdot}CH{\cdot}[CH(CO_2C_2H_5)_2]_2$, is produced by the union of ethylidenemalonic ester (p. 564) and sodium malonic ester.

Ethylenedimalonic ester, *butane-$\alpha\alpha\delta\delta$-tetracarboxylic ester*, $(CO_2C_2H_5)_2CH{-}CH_2{\cdot}CH_2{\cdot}CH(CO_2C_2H_5)_2$, is formed together with *cyclo*propanedicarboxylic ester (Vol. II) when ethylene bromide acts on sodium malonic ester (Ber. **19**, 2038).

Alkylbutanetetracarboxylic esters, Ber. **28**, R. 300, 464.

Trimethylenedimalonic ester, *pentane-$\alpha\alpha\epsilon\epsilon$-tetracarboxylic ester*, $(CO_2C_2H_5)_2{-}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH(CO_2C_2H_5)_2$, is formed, together with *cyclo*butane dicarboxylic ester (*q.v.*) in the action of trimethylene bromide on two molecules of sodium malonic ester.

It is noteworthy that the disodium derivatives of the alkylenedimalonic esters are converted by the action of bromine or iodine, or of CH_2I_2 and $CH_2Br{\cdot}CH_2Br$, into *cyclo*paraffintetracarboxylic esters. The alkylenedimalonic acids split off two CO_2-groups and yield alkylenediacetic acids; so, too, the *cyclo*paraffin tetracarboxylic acids, obtained from the alkylenedimalonic acids, yield *cyclo*paraffindicarboxylic acids:


Methylenedimalonic acid. *cyclo*Propanetetracarboxylic acid. *cyclo*Propanedicarboxylic acid.

Ethylenedimalonic acid. *cyclo*Butanetetracarboxylic acid. *cyclo*Butanedicarboxylic acid.

Trimethylenedimalonic acid. *cyclo*Pentanetetracarboxylic acid. *cyclo*Pentanedicarboxylic acid.

Propane-αββγ-tetracarboxylic acid, $(HO_2C)_2C(CH_2CO_2H)_2$, m.p. 151° with decomposition into CO_2 and tricarballylic acid (p. 647); *ethyl ester,* b.p. 295°/200 mm., is prepared from sodium ethanetricarboxylic ester and chloroacetic acid.

Tetracarboxylic acids are formed by the addition of sodium malonic and sodium alkylmalonic esters to the olefinedicarboxylic esters. These acids lose CO_2 and become tricarballylic acids (p. 647) (J. pr. Chem. [2] **35**, 349 : Ber. **24**, 311 : **24**, 2889 : **26**, 364). If citraconic ester be added to sodium malonic ester and sodium alkylmalonic ester, a further partial condensation takes place of the first-formed tetracarboxylic ester to *cyclo*butanonetricarboxylic ester (Vol. II) (Ber. **33**, 3742):

Propane-ααβγ-tetracarboxylic ester, $(CO_2C_2H_5)_2CH{\cdot}CH(CO_2C_2H_5){\cdot}CH_2CO_2C_2H_5$, b.p. 203°, is obtained (1) from fumaric ester and sodium malonic ester (*cf.* ethylidenedimalonic ester); (2) from monochlorosuccinic ester and sodium malonic ester (Ber. **23**, 3756 : **24**, 596). Tricarballylic acid is produced when the ester is hydrolysed with alcoholic potassium hydroxide.

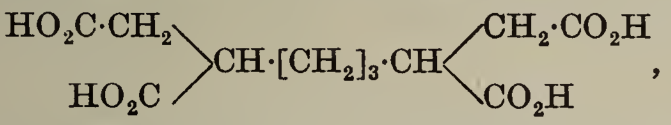
Pentane-αβγγ-tetracarboxylic ester is formed from sodium ethyl malonic ester and fumaric ester. It yields a *sodium* salt, $(C_2H_5O_2C)_2C(C_2H_5){\cdot}CH(CO_2C_2H_5){\cdot}CHNa(CO_2C_2H_5)$, which, with iodomethane, gives *hexane-βγδδ-tetracarboxylic ester* (*cf.* p. 646) (Ber. **33**, 3743).

αα-Dimethyl-β-cyanotricarballylic ester, b.p. 234°/25 mm., is prepared from sodium cyanosuccinic ester (p. 646) and bromo*iso*butyric ester (C. 1899, I. 826). Boiling dilute hydrochloric acid hydrolyses it to αα-dimethyltricarballylic acid (p. 647).

Butane-αβγδ-tetracarboxylic acid, $CH_2(CO_2H)CH(CO_2H)CH(CO_2H)CH_2(CO_2H)$, m.p. 244°, is prepared from α-malonic tricarballylic acid. Its *dianhydride,* m.p. 173° (Ber. **26**, 364 : **28**, 882).

Pentane-αβδε-tetracarboxylic acid, methylenedisuccinic acid, $CH_2[CH(CO_2H){\cdot}CH_2(CO_2H)]_2$, m.p. 216° (decomp.) (C. 1902, II. 733).

Heptane-αβζη-tetracarboxylic acid, trimethylenedisuccinic acid,

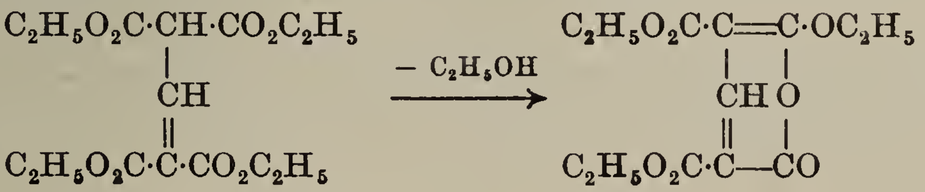


m.p. 159°, is produced when hydrochloric acid effects the hydrolysis of trimethylene dicyanosuccinic ester, the reaction product of trimethylene bromide and sodium cyanosuccinic ester (C. 1899, I. 326).

B. OLEFINETETRACARBOXYLIC ACIDS

Ethylenetetracarboxylic ester, $(C_2H_5O_2C)_2C{=}C(CO_2C_2H_5)_2$, m.p. 58°, b.p. 325°, is formed from disodium malonic ester and iodine; from chloromalonic ester and sodium ethoxide (Ber. **29**, 1290); and from bromomalonic ester and K_2CO_3 or tertiary bases (Ber. **32**, 860 : **34**, 2077).

Dicarboxyglutaconic acid, propylene-ααγγ-tetracarboxylic ester, methenylbismalonic ester, $(C_2H_5O_2C)_2CH{\cdot}CH{=}C(CO_2C_2H_5)_2$, is formed from sodium malonic ester and chloroform or carbon tetrachloride (Ber. **35**, 2881). It is an oil, which is converted by the action of piperidine in benzene solution into two *dimolecular modifications,* m.pp. 103° and 88°; these are transformed into the sodium salt of the ordinary ester by sodium alcoholate. The ester melting at 103° is hydrolysed by hydrochloric acid into the bimeric glutaconic acid, m.p. 207°, whilst the ordinary ester, similarly treated, yields the simple glutaconic acid, m.p. 139° (Ber. **34**, 675). Reduction with sodium amalgam produces the fluid dicarboxyl glutaric ester (p. 668). When heated it passes into the *δ-lactone,* m.p. 94°, by loss of alcohol (Ber. **22**, 1419 : **26**, R. 9 : Ann. **297**, 86).



Aqueous alkali hydroxide decomposes it into formic acid and malonic acid, together with glutaconic acid (p. 575) (Ber. **27**, 3061 : C. 1897, I. 29, 229) (*cf.* also *iso*aconitic acid (p. 648). Ammonia, hydrazine, and hydroxylamine causes the splitting-off of malonic ester from the dicarboxyglutaconic ester molecule and the formation of cyclic derivatives of hydroxymethylenemalonic ester (p. 615). Aniline combines with it at 0° in ethereal solution to form *β-anilinodicarboxyglutaric ester*, m.p. 46°, which, by further action of aniline, undergoes the decomposition described above (Ber. **30**, 1757, 2022). When sodium dicarboxyglutaconic ester is heated with alcohol to 150°, trimesic acid (Vol. II) is formed, a reaction which probably also depends on primary formation into hydroxymethylenemalonic acid (C. 1901, II. 822).

αγ-Dicyanoglutaconic ester, $\mathrm{EtO{\cdot}CO{\cdot}CH(CN){\cdot}CH : C(CN)COOEt}$, m.p. 178°, and *αγ-dicyanoglutaconic amide* are formed from chloroform or carbon tetrachloride and sodium cyanoacetic ester or sodium cyanoacetamide respectively (C. 1898, I. 29, 37 : Ber. **26**, 2881).

Propylene-αβγγ-tetracarboxylic acid. A derivative of this is *α-cyanoaconitic ester*, $\mathrm{CNCH(CO_2C_2H_5)C(CO_2C_2H_5) : CH(CO_2C_2H_5)}$, b.p. 215°/25 mm., which results from the reaction of cyanoacetic ester, oxaloacetic ester, and sodium alcoholate. The sodium salt of the ester and iodomethane give first *α-cyano-α-* or *-γ-methylaconitic ester*, b.p. 211°/25 mm., and then *α-cyano-αγ-dimethylaconitic ester*, $\mathrm{CN{\cdot}C(CH_3)(CO_2C_2H_5){\cdot}C(CO_2C_2H_5) : C(CH_3)CO_2C_2H_5}$, b.p. 206°/25 mm. (C. 1906, II. 21).

Butenetetracarboxylic ester, $\mathrm{CH_2(CO_2R)C(CO_2R)_2CH : CH(CO_2R)}$, b.p. 216-218°/14 mm., is formed from sodium isaconitic ester and bromoacetic ester (C. 1902, II. 722).

VII. THE PENTAHYDRIC ALCOHOLS AND THEIR OXIDATION PRODUCTS

1. PENTAHYDRIC ALCOHOLS, PENTITOLS

One of these, *adonitol*, occurs in nature ; all the rest have been obtained by the reduction of the corresponding aldopentoses with sodium amalgam. Their constitution follows from that of the aldopentoses from which they have been prepared (p. 672). The simplest pentitol, $C_5H_7(OH)_5$ or $CH_2{\cdot}OH{\cdot}\overset{*}{C}HOH{\cdot}CHOH{\cdot}\overset{*}{C}HOH{\cdot}CH_2OH$, can have five theoretical modifications, because in the formula two asymmetric carbon atoms are present, and they are separated by a non-asymmetric carbon atom. There are two optically active modifications, d- and l-*arabitol.* There is also an inactive resolvable modification, produced by the union of the preceding forms, and finally, there exist two optically inactive modifications due to internal compensation. These cannot be resolved, and are known as *xylitol* and *adonitol.* The pentitols are oxidized to pentoses by bromine and sodium hydroxide (Ber. 27, 2486). The stereochemical relations of the pentitols are shown on p. 703.

The number of possible classes of pentahydric alcohols is 21 ; that of the classes of substances which can be termed oxidation products of the pentitols is 55, if the hydroxy-compounds are not divided into sub-classes according to the character of the alcoholic hydroxyls, otherwise the number rises to 231.

1. **l-Arabitol,** $C_5H_7(OH)_5$, m.p. 102°, is lævorotatory after the addition of borax to its aqueous solution. It is produced by the reduction of ordinary or *l*-arabinose (p. 674), and has a sweet taste (Ber. **24**, 538, 1839 note). *Benzal arabitol*, m.p. 150° (Ber. **27**, 1535). *Diacetone arabitol*, b.p. 145–152°/23 mm. (Ber. **28**, 2533). ***d*-Arabitol** is dextrorotatory, and is produced by reduction of *d*-arabinose or *d*-lyxose. It combines with *l*-arabitol to form the racemic ***dl*-arabitol,** m.p. 106° (Ber. **32**, 555 : **33**, 1802).

2. **Xylitol,** $C_5H_7(OH)_5$, is syrup-like and optically inactive. It results from the reduction of xylose (p. 674) Ber. **24**, 538 : 1839 note : R. 567 : **27**, 2487).

3. **Adonitol,** $C_5H_7(OH)_5$, m.p. 102°, is optically inactive. It occurs in *Adonis vernalis*, and is produced by the reduction of ribose (p. 675) (Ber. **26**, 633). *Adonitol diformacetal*, m.p. 145° (Ber. **27**, 1893). *Adonitol diacetone*, b.p. 150–155°/17 mm.

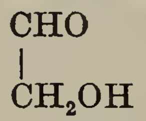
4. **Rhamnitol,** $CH_3{\cdot}C_5H_6(OH)_5$, m.p. 121°, is dextrorotatory ; it results from the reduction of rhamnose (p. 675 ; Ber. **23**, 3103). *Dimethylenerhamnitol*, $CH_3{\cdot}C_5H_6O_4(CH_2)_2OH$, m.p. 138° (Ann. **299**, 321).

Aminotetrols : *Arabinamine*, $CH_2OH[CH(OH)]_3CH_2NH_2$, m.p. 99°, is lævorotatory, and is formed from *l*-arabinose oxime (p. 674) by reduction with sodium amalgam. It is a strong base, and is reduced by hydriodic acid to *n*-amylamine.

Xylamine is prepared from xylose oxime, and is a colourless syrup (p. 674) (C. 1904, I. 579).

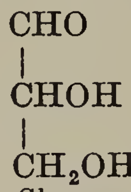
2. TETRAHYDROXYALDEHYDES, ALDOPENTOSES

The tetrahydroxyaldehydes, the first oxidation products of the pentahydric alcohols, are closely related to the pentahydroxyaldehydes or aldohexoses, the first class of the carbohydrates in the more restricted sense, and are very similar in chemical behaviour. Whereas formerly the carbohydrates occupied a special position in the province of aliphatic chemistry, they are now found to be very closely allied to simpler classes of bodies. All aldehyde- and ketone-alcohols, which can be regarded as the first oxidation products of the simplest representatives of the polyhydric alcohols, contain, like the carbohydrates in a narrower sense, in addition to carbon, hydrogen and oxygen in the same proportion as exist in water, *e.g.*:



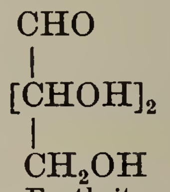
$$\begin{array}{l} CHO \\ | \\ CH_2OH \end{array}$$

Glycolyl aldehyde (Diose, $C_2H_4O_2$).



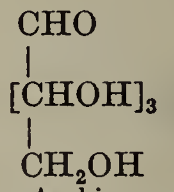
$$\begin{array}{l} CHO \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

Glycerose (Triose, $C_3H_6O_3$).



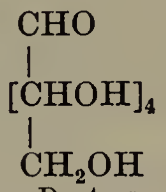
$$\begin{array}{l} CHO \\ | \\ [CHOH]_2 \\ | \\ CH_2OH \end{array}$$

Erythritose (Tetrose, $C_4H_8O_4$).



$$\begin{array}{l} CHO \\ | \\ [CHOH]_3 \\ | \\ CH_2OH \end{array}$$

Arabinose (Pentose, $C_5H_{10}O_5$).



$$\begin{array}{l} CHO \\ | \\ [CHOH]_4 \\ | \\ CH_2OH \end{array}$$

Dextrose (Hexose, $C_6H_{12}O_6$).

The simplest carbohydrates are the polyhydroxyaldehydes just mentioned, or ketone alcohols such as fructose, $CH_2OH{\cdot}[CHOH]_3{\cdot}CO{\cdot}CH_2OH$.

The aldopentoses show the following reactions in common with the hexoses: 1. They form *semiacetals* (*Glycosides*)* when condensed with alcohols by means of a small quantity of hydrochloric acid (Ber. **28**, 1156) (see p. 689).

1*b*. They condense with mercaptans in the presence of hydrochloric acid to form *mercaptals* (Ber. **29**, 547).

2. They form condensation products with aldehydes and with acetone in the presence of hydrochloric acid.

3. They are reduced by sodium amalgam to alcohols: pentitols.

4. Nitric acid oxidizes them to hydroxycarboxylic acids: tetrahydroxymono- and trihydroxydicarboxylic acids; they reduce Fehling's solution.

5. They yield osamines with methyl alcoholic ammonia (Ber. **28**, 3082).

6. Hydrazine converts the pentoses into aldazines (Ber. **29**, 2308).

7. Phenylhydrazine changes them to hydrazones and characteristic dihydrazones: *osazones*.

8. They yield oximes with hydroxylamine.

9. By successive treatment with hydrocyanic acid and hydrochloric acid they pass into pentahydroxyacids, the lactones of which may be reduced to hexoses (p. 682), whereby consequently the synthesis of a hexose from a corresponding pentose is realized.

However, the aldopentoses are (1) not fermented by yeast; (2) they yield furfuraldehyde or alkyl furfurals when they are distilled with hydrochloric acid or with dilute sulphuric acid. This reaction can be applied in the quantitative determination of the aldopentoses

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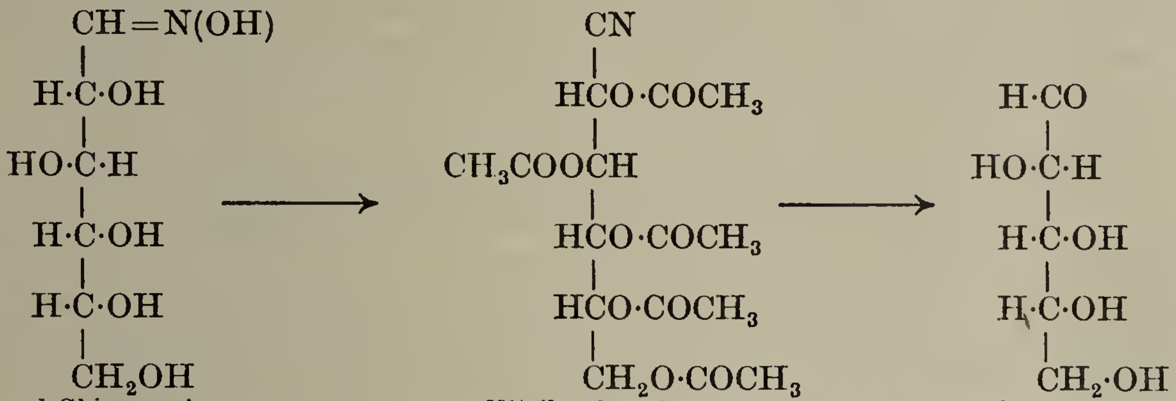
* It has been suggested that the sugar semiacetals should be, in general, termed *glycosides*, the term *glucoside* being reserved for those derived from glucose itself.

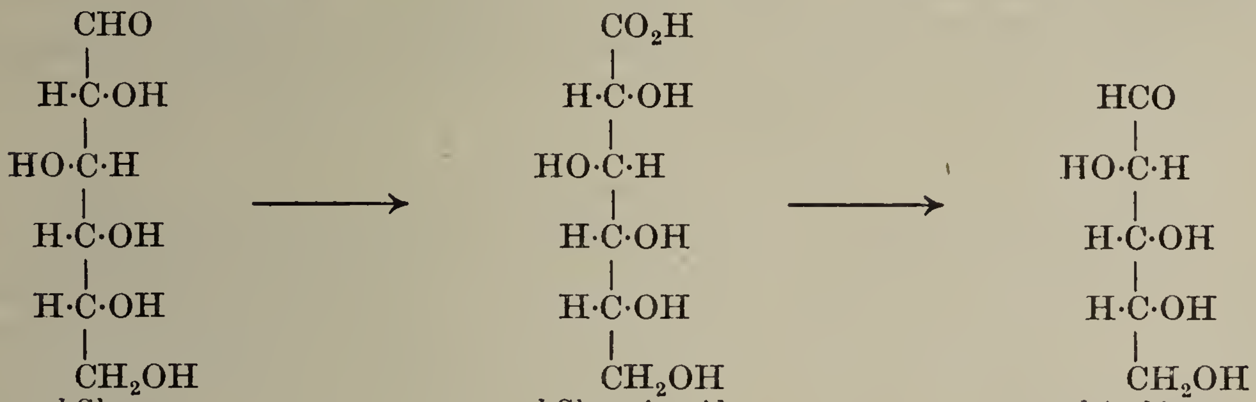
(Ber. **25**, 2912). (3) When they are heated with phloroglucinol and hydrochloric acid they give a cherry-red coloration (Ber. **29**, 1202).

Formation.—Their production from animal and vegetable sources will be indicated under the individual aldopentoses. However, a reaction will be given in this connection, which affords a general method for the conversion of aldohexoses into aldopentoses.

On treating *d*-glucoseoxime (p. 693) with acetic anhydride and sodium acetate, the nitrile of pentaacetylgluconic acid is obtained. This, when treated with ammoniacal silver solution gives up hydrocyanic acid, and is converted into *d*-arabinose diacetamide CH_2-$OH \cdot [CHOH]_3CH(NHAc)_2$ which on hydrolysis with hydrochloric acid yields *d*-arabinose (Ber. **26**, 737 : **32**, 3666).


d-Glucoseoxime. Nitrile of pentaacetylgluconic acid. *d*-Arabinose.

When *d*-glucose is oxidized with chlorine water it is converted into *d*-gluconic acid which is further changed by hydrogen peroxide in presence of ferric acetate into *d*-arabinose (Ber. **32**, 3672) :


d-Glucose. *d*-Gluconic acid. *d*-Arabinose.

d-Arabinose is the first aldopentose to be prepared synthetically, as it may be obtained from *d*-glucose (p. 692) which can be synthesized.

The two degradation methods described above have led to the following reactions : the production of *l*- and *d*-xylose from *l*- and *d*-gulonic acid (see below and p. 674) ; lyxose from galactose and galactonic acid (p. 675) ; *l*-erythritose and *l*-threose from *l*-arabinose and *l*-xylose (p. 651) ; *d*- and *l*-erythritose and *l*-threose from *l*- and *d*-arabonic acid and *l*-xylonic acid, etc.

The aldopentoses of the formula $CH_2OH \cdot \overset{*}{C}HOH \cdot \overset{*}{C}HOH \cdot \overset{*}{C}HOH \cdot$-CHO, containing three asymmetric carbon atoms, can appear theoretically in eight optically active isomers, and four optically active, racemic or *dl*-modifications which can be resolved (p. 703).

Constitution of Pentoses.—The constitution of the pentoses as represented with an internal oxide ring is based on the same arguments as those applicable to the hexoses and is discussed with the latter (p. 689).

1. **Arabinose.**—Ordinary arabinose contains a 1 : 5-amylene oxide ring (J.C.S., **127**, 358). Derivatives of the 1 : 4-butylene oxide structure, γ-arabinose, such as γ-methylarabinoside are also known (J.C.S. **127**, 367).

l-**Arabinose,** *pectinose*, m.p. 160°, is formed when cherry gum and other gums (p. 736) are boiled with dilute sulphuric acid (Ber. **35**, 1457 : **37**, 1210). **Reduction** produces *l*-arabitol (p. 671), and oxidation *l*-arabonic acid (p. 676) and *l*-**tri**hydroxyglutaric acid, m.p. 127° ; hydrochloric acid gives rise to furfural. It is *dextrorotatory*, $[\alpha]_D = +105{\cdot}25°$, and it reduces Fehling's solution. *Methyl*-l-*arabinoside*, $C_5H_9O_5{\cdot}CH_3$, m.p. 170° (Ber. **26**, 2407 : **28**, 1156), is prepared from arabinose, methyl alcohol and hydrochloric acid. The action of iodomethane and silver oxide produces methylation of the OH-groups, forming *trimethylmethylarabinoside*, m.p. 44°, b.p. 124°/14 mm. Hydrochloric acid hydrolyses this substance to *trimethylarabinose*, $(CH_3O)_3C_5H_7O_2$, b.p. 148–152°/19 mm. (C. 1906, II. 1045).

l-*Arabinosazone*, $C_5H_8O_3(N_2HC_6H_5)_2$, m.p. 160° (Ber. **24**, 1840, footnote). *Arabinosone* (Ber. **24**, 1840, footnote ; C. 1904, I. 579). l-*Arabinose*-p-*bromophenylhydrazone*, m.p. 150–155° (Ber. **27**, 2490). l-*Arabinose semicarbazone*, m.p. 163° (decomp.) (C. 1897, II. 894). l-*Arabinose oxime*, m.p. 133° (Ber. **26**, 743), can be degraded to *l*-erythritose (p. 650), and reduced to *l*-arabinamine (p. 671). *Arabinose ethyl mercaptal*, m.p. 125°. *Arabinose ethylene mercaptal*, m.p. 154°. *Arabinose trimethylene mercaptal*, m.p. 150° (Ber. **29**, 547). *Arabinochloral*, α-form, m.p. 124° ; β-form, m.p. 183°. *Arabinobromal*, $C_5H_8O_5{\cdot}CH{\cdot}CBr_3$, m.p. 210° (Ber. **29**, R. 544). *Arabinose diacetone*, m.p. 42° (Ber. **28**, 1164). *Arabinose tetranitrate*, m.p. 85° (Ber. **31**, 71). *Acetochloroarabinose*, $C_5H_6Cl(OCOCH_3)_3$, m.p. 149°, and *acetobromoarabinose*, $C_5H_6Br(OCOCH_3)_3$, m.p. 137°, are prepared from arabinose and acetyl chloride and bromide respectively. Silver acetate converts them into *tetraacetylarabinose*, $C_5H_6O(OCOCH_3)_4$, m.p. 80° (C. 1902, I. 911). *Tetracarbomethoxyarabinose*, m.p. 123°, $[\alpha]_D - 126{\cdot}6°$, is obtained from arabinose, chloroformic ester and absolute pyridine (J.C.S. **1926**, 1752).

l-*Arabinal*, m.p. 81–83°, $[\alpha]_D - 202{\cdot}8°$, is obtained by reduction of triacetylbromoarabinose with zinc dust and 50% acetic acid, and corresponds in structure to glucal (p. 696) (Ber. **60**, 918).

l-*Arabinodesose* (1-2-*desoxyarabinose*), m.p. *ca* 90°, is formed from arabinal by contact with dilute acids at 0° (Ber. **60**, 918).

d-**Arabinose** is prepared (1) by degradation of *d*-dextrose oxime ; from the reaction product it is best separated as the *diphenylhydrazone*, $C_4H_5(OH)_4CH:NH(C_6H_5)_2$, which is decomposed by formaldehyde (C. 1902, I. 985) ; (2) by oxidation of *d*-gluconic acid by H_2O_2 (above), or by heating a solution of mercuric *d*-gluconate (C. 1908, I. 1166). It is *lævorotatory*, $[\alpha]_D = -105°$. d-*Arabinosazone*, m.p. 160°. d-*Arabinose diacetamide*, $C_5H_{10}O_4(NH{\cdot}COCH_3)_2$, m.p. 187°.

dl-**Arabinose,** m.p. 164°, is produced by the union of the two optically active forms of arabinose. It is one of the sugars found in the urine of a sufferer from *pentosuria*. This is of interest, since, so far, only optically active sugars have been found to be produced as a result of metabolism. It can be resolved by *as.-d*-amyl phenylhydrazine (Ber. **38**, 868). dl-*Arabinosazone*, m.p. 167° (Ber. **33**, 2243).

Derivatives of γ-Arabinose (1 : 4-oxide ring).—*γ-Methylarabinoside*, a syrup showing mutarotation, $[\alpha]_D - 1°$ to $- 42°$, is obtained from arabinose and methyl alcoholic hydrogen chloride at 18°. *Trimethyl-γ-methylarabinoside*, b.p. 85–87°/0·3 mm., $[\alpha]_D - 55{\cdot}8°$ (in water). *Trimethyl-γ-arabinose*, b.p. 97–99°/0·18 mm., $[\alpha]_D - 39{\cdot}5°$ (in water) (J.C.S. **127**, 367).

2. **Xylose.** (Presence of amylene oxide ring, see J.C.S. **123**, 1352.)

l-**Xylose,** *wood sugar*, $C_4H_5(OH)_4{\cdot}CHO$, m.p. 143°, is produced when wood gums (Ber. **22**, 1047 : **23**, R. 15 : C. 1902, I. 301), corn-cobs (Ber. **24**, 1657), maize, or elder pith (Ber. **35**, 1457) are boiled with dilute acids ; by the degradation of *l*-gulonic acid (p. 714) by hydrogen peroxide (Ber. **33**, 2142) ; also, by pancreatic hydrolysis of nucleo-proteins (Ber. **35**, 1467). It is *dextrorotatory*, and yields inactive xylitol (p. 671) on reduction ; oxidation converts it into *l*-xylonic acid (p. 676) and inactive trihydroxyglutaric acid, m.p. 152°. Hydrocyanic acid produces *l*-gulonic acid and *l*-idonic acid (p. 714). l-*Xylosazone*, m.p. 160°.

d-**Xylose** is obtained from *d*-gulonic lactone by degradation. It is *lævorotatory* (Ber. **33**, 2145). dl-*Xylosazone*, m.p. 210–215°, with decomposition (Ber. **27**, 2488 : **33**, 2145). *Methylxyloside*, $C_5H_9O_5{\cdot}CH_3$, α-, m.p. 91° ; β-, m.p. 156° (Ber. **28**, 1157). *Xylochloral*, m.p. 132° (Ber. **28**, R. 148).

3. **Lyxose**, m.p. 101°, is prepared by reduction of lyxonic lactone (p. 676) ; from pentaacetylgalactonic nitrile by loss of hydrocyanic acid (Ber. **30**, 3103) ; and from *d*-galactonic acid and H_2O_2 (Ber. **33**, 1798). Addition of hydrocyanic acid and hydrolysis produces galactonic and talonic acids (Ber. **33**, 2146).

4. **Ribose**, $C_4H_5(OH)_4CHO$, is produced by oxidation of *l*-arabinose to *l*-arabonic acid, conversion of this into ribonic acid (p. 676) and reduction of the lactone of this acid (Ber. **24**, 4220).

Preparation of d-*ribose*, C. 1913, II, 1562. Ribose is a component of pancreas and liver nucleoproteins (see nucleic acids, p. 748). It is identified by means of its *dihydrazone*, m.p. 141–142°, with diphenylmethanedimethyldihydrazine, $CH_2{\cdot}(C_6H_4{\cdot}NMe{\cdot}NH_2)_2$ (Ber. **46**, 3949).

5. **Apiose**, *β-hydroxymethylerythritose*, $(CH_2OH)_2C(OH)CH(OH)CHO$, is prepared by hydrolysis of *apiin*, a glucoside occurring in parsley (Vol. II). It differs from the isomeric pentoses by reason of its branched carbon chain. Oxidation with bromine water produces tetrahydroxy*iso*valeric acid (Ann. **321**, 71). *Osazone*, m.p. 156° (C. 1902, I. 912).

6. **Rhamnose**, or iso*dulcitol*, $CH_3(CHOH)_4CHO + H_2O$, m.p. 93°, (Ring structure, see J.C.S. **1926**, 22 : Ber. **59**, 836) in anhydrous form ; m.p. 122–126° when crystallized from acetone. It is *dextrorotatory* (Ber. **29**, R. 117, 340). It results upon decomposing different glucosides (*quercitrin*, *xanthorhamnin*, *rhamninose*, a disaccharide, derived from galactose and rhamnose (C. 1900, I. 251), *hesperidin*, *naringin*) with dilute sulphuric acid. It yields α-methylfurfural when distilled with sulphuric acid (Ber. **22**, R. 751).

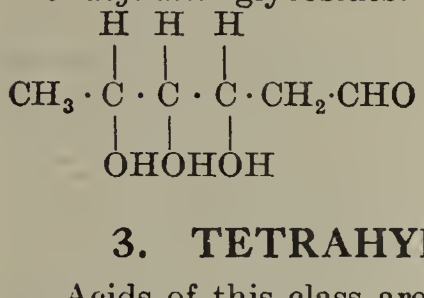
It gives rise to rhamnitol upon reduction, and by oxidation *l*-trihydroxyglutaric acid (m.p. 127°). HCN and hydrochloric acid convert it into rhamnose carboxylic acid (p. 714 : Ber. **22**, 1702) ; the *oxime* has been decomposed into methyl tetrose (p. 651 : Ber. **29**, 1378) ; *hydrazone*, m.p. 159°, and *osazone*, m.p. 180° (Ber. **20**, 2574). *Acetone rhamnose*, $C_6H_{10}O_5 : C_3H_6$, m.p. 90° (Ber. **28**, 1162). *Rhamnose ethyl mercaptal*, m.p. 136°. *Ethylene mercaptal*, m.p. 169° (Ber. **29**, 547). *Tetranitrate*, m.p. 135° (Ber. **31**, 71).

7. *iso***Rhamnose** has been obtained by the reduction of the lactone of *iso*rhamnonic acid.

8. **Chinovose**, $CH_3[CHOH]_4CHO$, isomeric with rhamnose, is a product obtained by decomposing chinovin, occurring in varieties of quina and cinchona with hydrochloric acid. *Osazone*, m.p. 193–194° (Ber. **26**, 2417).

9. **Rhodeose**, $CH_3[CH(OH)]_4CHO$, is one of the methylpentoses obtained by decomposing the pentosides *convovulin* and *jalapin* (Vol. II). It is strongly dextrorotatory, and is the optical antipode to **fucose**. This substance is obtained by hydrolysis of the *Fucus* variety of sea-weeds with dilute sulphuric acid. *Osazone*, m.p. 177°. Determination of configuration (Ber. **40**, 2434).

10. **Digitoxose**, $CH_3{\cdot}[CHOH]_3{\cdot}CH_2{\cdot}CHO$, is a desoxyhexose occurring in the *digitalis* glycosides. Its configuration has recently been established as



$$CH_3\cdot\underset{OH}{\overset{H}{C}}\cdot\underset{OH}{\overset{H}{C}}\cdot\underset{OH}{\overset{H}{C}}\cdot CH_2\cdot CHO$$

(Ber. **55**, 75 : **63**, 347).

3. TETRAHYDROXYMONOCARBOXYLIC ACIDS

Acids of this class are obtained by oxidizing the aldopentoses with bromine water or dilute nitric acid. They readily pass into lactones, some of which yield pentoses on reduction. Furthermore, oxidation changes them in part to dicarboxylic acids. Hydriodic acid reduces some of them to lactones of the monohydroxyparaffincarboxylic acids. All the known acids are optically active.

Tetrahydroxy-*n*-valeric acids, like the aldopentoses, occur in eight optically active forms, five of which are known, and four *dl*-modifications.

(1) ***l*-Arabonic acid,** $CO_2H[CHOH]_3CH_2OH$, $[\alpha]_D^{20} = -73{\cdot}9°$, is prepared from *l*-arabinose (Ber. **21**, 3007). It readily yields a *lactone*, $C_5H_8O_5$, m.p. 95–98°, and is converted by oxidation into l-*trihydroxyglutaric acid*; *phenylhydrazide*, m.p. 215° (Ber. **23**, 2627 : **24**, 4219). *Tetraacetyl*-l-*arabonic nitrile*, m.p. 117°, is produced from *l*-arabinose oxime, acetic anhydride, and sodium acetate. Silver oxide changes it into triacetyl-*l*-erythrose (Ber. **32**, 3666).

***d*-Arabonic acid,** $[\alpha]_D^{20} = +73{\cdot}7°$, is formed from *d*-arabinose and bromine water; *lactone*, m.p. 98°. Oxidation by H_2O_2 converts it into *d*-erythritose.

dl-*Arabonic lactone*, m.p. 116° (Ber. **32**, 556).

When heated to 145° with aqueous pyridine *l*-arabonic acid yields pyromucic acid, together with some

(2) ***l*-Ribonic acid,** which, under the same conditions, is partially reconverted into arabonic acid. *Ribonic lactone*, $C_3H_3O_5$, m.p. 72–76° (Ber. **24**, 4217); *phenylhydrazide*, m.p. 163°.

(3) ***l*-Xylonic acid** is prepared from *l*-xylose and bromine. It yields a sparingly soluble bromocadmium double salt (*cf.* Ber. **35**, 1473). Pyridine converts it into

(4) ***d*-Lyxonic acid**; *lactone*, m.p. 113° (Ber. **30**, 3107) (see also Lyxose, p. 675); *phenylhydrazide*, m.p. 162°.

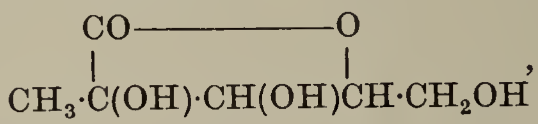
(5) **Apionic acid,** *tetrahydroxy*iso*valeric acid*, $(CH_2OH)_2C(OH)CH(OH)$-$COOH$, is produced from apiose (p. 675) and bromine water. *Phenylhydrazide*, m.p. 127°, is converted by hydriodic acid and phosphorus into *iso*valeric acid (Ann. **321**, 78).

(6) **Rhamnonic acid** is formed from rhamnose and bromine, and passes directly into the *lactone*, $C_6H_{10}O_5$, m.p. 150° (Ber. **23**, 2992 : Ann. **271**, 73). *Methylene rhamnonic lactone*, $C_6H_8(CH_2)O_5$, m.p. 179° (Ann. **309**, 323). When heated with pyridine to 150° it yields some

(7) ***iso*Rhamnonic acid,** of which the *lactone*, m.p. 151°, when oxidized yields xylotrihydroxyglutaric acid (p. 677) (Ber. **29**, 1961).

(8) **Saccharic acids** is the name given to a number of tetrahydroxypentanecarboxylic acids which are obtained from the hexoses or disaccharides by the action of alkalis, or, better, lime-water, accompanied by atomic migration. They readily pass into *lactones*, known as *saccharins*, which must not be confused with saccharine (Vol. II), a sweetening agent entirely unconnected with sugars and their associated compounds.

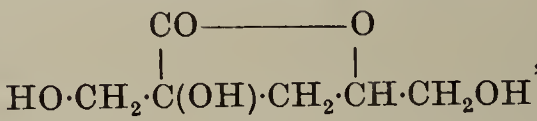
Saccharin,



$$\begin{array}{l}\qquad\ \ \mathrm{CO}\text{—————}\mathrm{O}\\ \qquad\ \ \ |\qquad\qquad\qquad |\\ \mathrm{CH_3{\cdot}C(OH){\cdot}CH(OH)CH{\cdot}CH_2OH}\end{array}$$

, m.p. 160°, possesses a bitter taste.

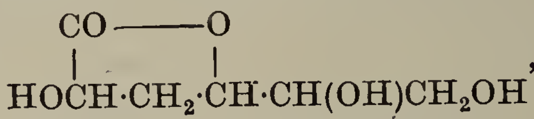
iso*Saccharin*,



$$\begin{array}{l}\qquad\qquad\ \mathrm{CO}\text{————}\mathrm{O}\\ \qquad\qquad\ \ |\qquad\qquad |\\ \mathrm{HO{\cdot}CH_2{\cdot}C(OH){\cdot}CH_2{\cdot}CH{\cdot}CH_2OH}\end{array}$$

, m.p. 95°.

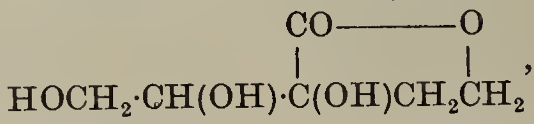
Metasaccharin,



$$\begin{array}{l}\quad\ \mathrm{CO}\text{——}\mathrm{O}\\ \quad\ \ |\qquad\ \ |\\ \mathrm{HOCH{\cdot}CH_2{\cdot}CH{\cdot}CH(OH)CH_2OH}\end{array}$$

, m.p. 141°.

Parasaccharin,



$$\begin{array}{l}\qquad\qquad\qquad\quad\ \mathrm{CO}\text{———}\mathrm{O}\\ \qquad\qquad\qquad\quad\ \ |\qquad\quad\ |\\ \mathrm{HOCH_2{\cdot}CH(OH){\cdot}C(OH)CH_2CH_2}\end{array}$$

, a syrup.

Saccharin is produced by the action of lime-water on dextrose, lævulose and invert sugar; *iso*-, meta-, and para-saccharin from lactose or galactose and lime-water. When reduced with hydriodic acid, saccharin and *iso*saccharin yield $\alpha\gamma$-dimethylbutyrolactone, whilst metasaccharin gives γ-*n.*-caprolactone. Nitric acid converts saccharin into α-methyltrihydroxyglutaric acid (*saccharonic acid*); *iso*saccharin into $\alpha\gamma$-dihydroxyglutaric-γ-carboxylic acid, $(HO_2C)_2C(OH)CH_2CH$-$(OH)CO_2H$; metasaccharin into $\alpha\beta\delta$-trihydroxyadipic acid (see below); and parasaccharin to parasaccharonic acid and hydroxycitric acid (p. 678), H_2O_2 (p. 673) brings about the degradation of *iso*- and para-saccharine to two ketopentanetriols, $HOCH_2{\cdot}COCH_2CH(OH)CH_2OH$, and $HOCH_2{\cdot}CH(OH){\cdot}CO{\cdot}CH_2CH_2$-$OH$, respectively; metasaccharin gives an aldotriose, *metasaccharopentose*, $HOC{\cdot}CH_2CH(OH)CH(OH)CH_2OH$, the aldehyde of a $\beta\gamma\delta$-trihydroxyvaleric acid, which is reduced by hydriodic acid to γ-valerolactone (Ann. **218**, 373 : **299**, 323 : Ber. **18**, 631, 2514 : **35**, 2361 : **37**, 3612 : **38**, 2671 : **41**, 158).

4. TRIHYDROXYDICARBOXYLIC ACIDS

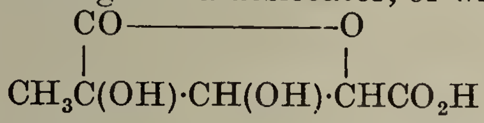
Trihydroxy-*n*.-glutaric acids, $CO_2H[CHOH]_3CO_2H$, can theoretically exist in four stereochemical modifications, corresponding with the four pentitols (p. 703), and in addition in an inactive form which can be resolved.

d-*Trihydroxyglutaric acid,* d-*arabotrihydroxyglutaric acid,* m.p. 127°, is prepared from *d*-arabinose and nitric acid. l-*Trihydroxyglutaric acid,* m.p. 127°, is formed from *l*-arabinose and nitric acid, as well as by the oxidation of rhamnose (p. 675) and sorbinose (p. 699) (Ber. **21**, 3276). dl-*Trihydroxyglutaric acid,* m.p. 154°, results from the union of *d*- and *l*-trihydroxyglutaric acid in acetone solution (Ber. **32**, 558).

i-*Xylotrihydroxyglutaric acid,* m.p. 152°, is formed when xylose is oxidized; it corresponds with xylitol (p. 671). It is similar to, but not identical with, the racemic acid (Ber. **32**, 559).

i-*Ribotrihydroxyglutaric acid* results from the oxidation of ribose, and corresponds with adonitol (p. 671). It readily passes into a *lactonic acid,* $C_3H_6O_6$, m.p. 170° (Ber. **24**, 4222).

Ethers.—d-*Arabotrimethoxyglutaric acid* is obtained by the oxidation of trimethyl-α-methylarabinoside with nitric acid, and is identified as the *diamide,* m.p. 232–233° $[\alpha]_D + 50°$ (J.C.S. **127**, 358). *Xylo-trimethoxyglutaric* acid is similarly obtained by the oxidation of trimethylmethylxyloside and tetramethylglucose: its *amide,* m.p. 194°, is optically inactive (J.C.S. **1926**, 350).

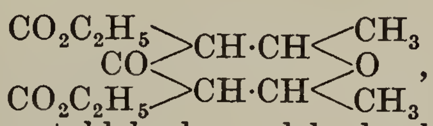
Saccharonic acid, *α-trihydroxy-α-methylglutaric acid,* $CH_3C(OH)(CO_2H)$-$CH(OH)CH(OH)(CO_2H)$, is formed by the oxidation of saccharin (see above) with nitric acid. It changes in a desiccator, or when heated, into a lævorotatory lactone, *saccharone,*  $\begin{array}{l}CO\text{———————}O\\ |\qquad\qquad\qquad\ |\\ CH_3C(OH){\cdot}CH(OH){\cdot}CHCO_2H\end{array}$, m.p. 145–156° (Ann. **218**, 363).

Hydriodic acid converts the lactone into α-methylglutaric acid (p. 558).

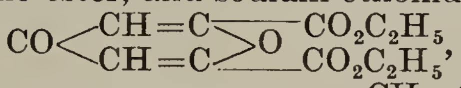
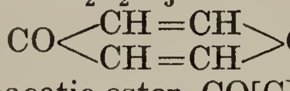
Trihydroxyadipic acid, $CO_2HCH(OH)CH_2CH(OH)CH(OH)CO_2H$, m.p. 146° with decomposition, results from the oxidation of metasaccharin (see above) with dilute HNO_3 (Ber. **18**, 1555: **37**, 2668). Heated with HI it is reduced to adipic acid.

5. DIHYDROXYKETONEDICARBOXYLIC ACIDS

The pyrone dicarboxylic esters, resulting from the condensation of acetone dicarboxylic esters with aldehydes, are cyclic anhydrides of the dihydroxyketonedicarboxylic acids.

Dimethyltetrahydropyronedicarboxylic ester,  , m.p. 102°, is formed from acetonedicarboxylic ester, acetaldehyde, and hydrochloric acid (Ber. **29**, 994).

6. TRIKETONEDICARBOXYLIC ACIDS

Acetonedioxalic ester, diethylxanthochelidonic ester, $CO[CH_2CO{\cdot}CO_2C_2H_5]_2$, m.p. 104°, is obtained from acetone, oxalic ester, and sodium ethoxide. Hydrochloric acid converts it into *chelidonic ester,* , m.p. 63°. Other acids, allied with this, are also derived from pyrone,  (Vol. II), such as a product of dehydration of carbonyl diacetoacetic ester, $CO[CH(COCH_3)$-$CO_2C_2H_5]_2$, prepared from copper acetoacetic ester and phosgene (Ber. **19**, 19).

7. DIHYDROXYTRICARBOXYLIC ACIDS

Desoxalic acid, $CO_2H{\cdot}CHOH{\cdot}C(OH)(CO_2H)_2$, is a deliquescent crystalline mass; *triethyl ester*, $CO_2C_2H_5{\cdot}CHOH{\cdot}C(OH){\cdot}(CO_2C_2H_5)_2$, m.p. 78°, b.p. 156°/2 mm., results from the action of sodium amalgam on diethyl oxalate (Ann. **297,** 96). When its aqueous solution is evaporated, or when its ester is heated with water or dilute acids to 100°, the acid yields carbon dioxide and racemic acid. (p. 655):

$$\underset{\text{Desoxalic acid.}}{HO_2C{\cdot}CH(OH)C(OH)(CO_2H)_2} \longrightarrow \underset{\text{Racemic acid.}}{HO_2C{\cdot}CH(OH)CH(OH)CO_2H} + CO_2.$$

Acid radicals can be substituted for the two hydroxyl groups of the desoxalic ester. Heated with hydriodic acid, desoxalic acid gives off carbon dioxide, and is reduced to succinic acid.

Desoxalic ester and phenylhydrazine yield glyoxylic ester phenylhydrazone, whilst *iso*nitrosomalonic ester and glycollic acid are the products of reaction with hydroxylamine (Ber. **29,** R. 908).

Hydroxycitric acid, *$\alpha\beta$-hydroxytricarballylic acid*, $CO_2HCH_2C(OH)(CO_2H)$-$CH(OH)CO_2H$, m.p. 160°, accompanies aconitic, tricarballylic, and citric acids in beet juice, and is produced by boiling chlorocitric acid (from aconitic acid and HClO) with alkalis or water (Ber. **16,** 1078). It can be obtained pure by oxidation of parasaccharin (p. 676) with nitric acid (Ber. **37,** 3614).

$\alpha\gamma$-Dihydroxypropane-$\alpha\alpha\gamma$-tricarboxylic acid, *$\alpha\gamma$-dihydroxyglutaric-γ-carboxylic acid*, $(CO_2H)_2C(OH)CH_2CH(OH)COOH$, results from the oxidation of *iso*saccharin with nitric acid. It is a thick crystalline mass. At 100° it loses carbon dioxide, and forms $\alpha\gamma$-dihydroxyglutaric acid. Hydriodic acid and phosphorus convert it into glutaric acid, $C_3H_6(CO_2H)_2$ (Ber. **38,** 2671).

8. PENTACARBOXYLIC ACIDS

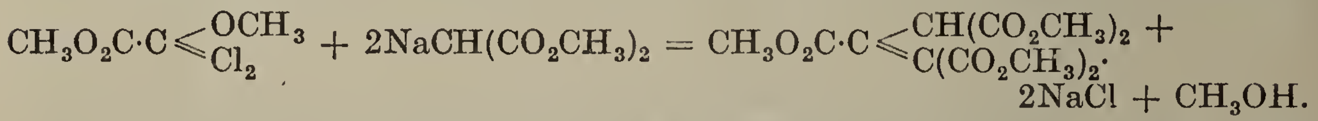
Paraffin Pentacarboxylic Acids.—*Propane-$\alpha\alpha\beta\beta\gamma$-pentacarboxylic acid, $\alpha\beta$-dicarboxytricarballylic acid*, $(CO_2H)_2CH{\cdot}C(CO_2H)_2{\cdot}CH_2CO_2H$, m.p. 150°, is obtained from its *penta-ethyl ester*, the reaction product of sodium malonic ester and chloroethanetricarboxylic ester (p. 646).

Propane-$\alpha\alpha\beta\gamma\gamma$-pentacarboxylic methyl ester, $\alpha\gamma$-dicarboxytricarballylic ester, $CH_3O_2C{\cdot}CH[CH(CO_2CH_3)_2]_2$, m.p. 86°, is prepared from dichloroacetic ester and two molecules of sodium malonic ester; also, by reduction of dicarboxyaconitic ester (see below) with zinc and glacial acetic acid (Ann. **347,** 5).

Butane-$\alpha\alpha\beta\gamma\gamma$-pentacarboxylic methyl ester, $\alpha\gamma$-dicarboxy-α-methyltricarballylic ester, $(CH_3O_2C)_2{\cdot}CH{\cdot}CH(CO_2CH_3){\cdot}C(CH_3)({\cdot}CO_2CH_3)_2$, m.p. 59°, is obtained by reduction of dicarboxymethylaconitic ester. These esters yield tricarballylic or the stereoisomeric α-methyltricarballylic acids on hydrolysis and expulsion of CO_2.

Butane-$\alpha\beta\beta\gamma\delta$-pentacarboxylic ester, $C_2H_5O_2C{\cdot}CH_2CH(CO_2C_2H_5)C(CO_2C_2H_5)_2{\cdot}$-$CH_2CO_2C_2H_5$, b.p. 217°/16 mm., is formed from chlorosuccinic ester and sodium ethenyl tricarboxylic ester.

Olefine Pentacarboxylic Acids: *Dicarboxyaconitic pentamethyl ester*, $(CH_3O_2C)_2{\cdot}C : C(CO_2CH_3){\cdot}CH(CO_2CH_3)_2$, m.p. 62°, is formed by condensation of dichlorooxalic methyl ester and two molecules of sodium malonic methyl ester, instead of the expected dicarboxy-methyl-citric ester, which loses methyl alcohol:



$$CH_3O_2C{\cdot}C{<}\begin{matrix}OCH_3\\Cl_2\end{matrix} + 2NaCH(CO_2CH_3)_2 = CH_3O_2C{\cdot}C{<}\begin{matrix}CH(CO_2CH_3)_2\\C(CO_2CH_3)_2{\cdot}\end{matrix} + 2NaCl + CH_3OH.$$

The ester, when hydrolysed, loses CO_2, and yields aconitic acid; with sodium and iodomethane it forms *α-methyldicarboxyaconitic ester, butylene-$\alpha\alpha\beta\gamma\gamma$-pentacarboxylic ester*, $CH_3C(CO_2CH_3)_2C(CO_2CH_3) : C(CO_2CH_3)_2$, m.p. 86° (Ann. **347,** 1).

Δ^{α}-Butylene-$\alpha\beta\gamma\gamma\delta$-pentacarboxylic ester, $C_2H_5O_2C{\cdot}CH_2{\cdot}C(CO_2C_2H_5)_2C(CO_2C_2$-$H_5) : CHCO_2C_2H_5$, b.p. 230°/10 mm., is prepared from sodium ethenyl tricarboxylic ester and chlorofumaric ester (Ber. **31,** 47). *Butylene-$\alpha\alpha\gamma\gamma\delta$-pentacarboxylic ester*, $C_2H_5O_2C{\cdot}CH_2C(CO_2C_2H_5)_2CH : C(CO_2C_2H_5)_2$, b.p. 224°/12 mm., is formed from sodium dicarboxyglutaconic ester (p. 669) and chloroacetic ester (J. pr. Chem. [2] **66,** 1, 104).

VIII. HEXA- AND POLY-HYDRIC ALCOHOLS AND THEIR OXIDATION PRODUCTS

I. POLYHYDRIC ALCOHOLS

1 A. HEXAHYDRIC ALCOHOLS, HEXAHYDROXYPARAFFINS, HEXITOLS

The hexahydric alcohols approach the first class of sugars (p. 683)—the monosaccharides—very closely. They resemble them in properties; they have a very sweet taste, but they do not reduce an alkaline copper solution, and are not normally fermented by yeast (*cf.*, however, Z. physiol. Chem. **173,** 72). *d*-Mannitol, *d*-sorbitol, and dulcitol occur in nature. These three and other hexitols have been prepared by the reduction of the corresponding hexoses—aldo- and keto-hexoses—with sodium amalgam. Moderate oxidation converts them into dextroses. The condensation products which the hexitols yield with aldehydes, especially formaldehyde and benzaldehyde, and with acetone, in the presence of hydrochloric acid or sulphuric acid, are characteristic of them (Ann. **299,** 316 : Ber. **27,** 1531 : **28,** 2531).

Theory requires the existence of 28 classes of hexahydroxyparaffin alcohols, which give rise to 79 classes of oxidation products, if the hydroxy compounds are included with those of the glycol oxidation products. The total number of sub-classes of oxidation compounds amounts to 434, of which 28 are free from alcoholic hydroxyls.

The simplest hexitols with six carbon atoms contain four asymmetric carbon atoms in the molecule. According to the theory of *van 't Hoff* and *Le Bel*, 10 simple spacial isomeric forms are possible for such a compound.

1. **Mannitol** or **mannite,** $CH_2OH[CHOH]_4CH_2OH$, exists in three modifications: *dextro-*, *lævo-*, and inactive mannitol; the latter is identical with the *α-acritol* made from synthetic *α-acrose* or *dl*-fructose. It is the parent substance for the synthesis of numerous derivatives of the mannitol series (Ber. **23,** 373), and also of glucose (p. 692) and of fructose (p. 698), as will be more fully explained under these bodies.

Ordinary, or *d*-**mannitol** (configuration, p. 704), m.p. 166°, occurs frequently in plants and in the manna-ash (*Fraxinus ornus*), the dried sap of which is *manna*. It is obtained from the latter by extraction with alcohol and allowing the solution to crystallize. It is produced in the ropy fermentation of the different varieties of sugar, and may be artificially prepared by the action of sodium amalgam on *d*-mannose (p. 691) or *d*-fructose, together with sorbitol (Ber. **17,** 127 : **23,** 3684).

Mannitol crystallizes from alcohol in delicate needles, and from water in large rhombic prisms. It possesses a very sweet taste. Its solution is dextrorotatory in the presence of borax. When oxidized with care by nitric acid, it yields fructose (previously known as mannitose) (Ber. **20**, 831), and *d*-mannose (Ber. **21**, 1805). More vigorous oxidation with nitric acid produces *d*-mannosaccharic acid (Ber. **24**, R. 763) (p. 717), erythritic acid, and oxalic acid. Hydriodic acid converts it into β- and γ-hexyl iodide (Ber. **40**, 140).

When mannitol is heated to 200° it loses water and forms the anhydrides, *mannitan*, $C_6H_{12}O_5$, and *mannide*, $C_6H_{10}O_4$, m.p. 87°, b.p. 176°/30 mm. The latter is also obtained by distilling mannitol in a vacuum.

Esters.—Mannitol dichlorohydrin, $C_6H_8Cl_2(OH)_4$, m.p. 174°, is formed when *d*-mannitol is heated with concentrated hydrochloric acid. Hydrobromic acid yields the *dibromohydrin*, m.p. 178°.

Nitromannitol, mannitol hexatetranitrate, $C_6H_8(O{\cdot}NO_2)_6$, m.p. 113°, is obtained by dissolving mannitol in a mixture of concentrated nitric and sulphuric acids. It crystallizes from alcohol and ether in bright needles ; it melts when carefully heated and deflagrates strongly. When struck it explodes very violently. Alkalis and ammonium sulphide regenerate mannitol. Ammonia, or, better, pyridine, acting on hexanitromannitol, produces *pentanitromannitol*, m.p. 82° (C. 1901, II. 983 : Ber. **36**, 794).

d-*Mannitol hexaacetate*, $C_6H_6(OCOCH_3)_6$, m.p. 119° (Ber. **12**, 2059), when left in contact with liquid HCl, changes into *tetraacetylmannitol dichlorohydrin*, $C_6H_8(C_2H_3O_2)_4Cl_2$, m.p. 214° (Ber. **35**, 842).

Hexabenzoyl mannitol, m.p. 149°.

Mannitol triformal, $C_6H_8O_6(CH_2)_3$, m.p. 227° (Ann. **289**, 20).

Mannitol tribenzal, $C_6H_8O_6(CHC_6H_5)_3$, m.p. 213–217° (Ber. **28**, 1979).

Mannitol triacetone, $C_6H_8O_6(C_3H_6)_3$, m.p. 69°, is obtained from mannitol, acetone, and a little hydrochloric acid. It has a bitter taste (Ber. **28**, 1168).

l-**Mannitol**, m.p. 163–164°, is obtained by the reduction of *l*-mannose (from *l*-arabinose carboxylic acid, p. 712) in weak alkaline solution with sodium amalgam (Ber. **23**, 375). It is quite similar to ordinary mannitol, and in the presence of borax is lævorotatory.

Inactive **mannitol**, dl-*mannitol*, m.p. 168°, is produced in a similar manner, from inactive mannose (from *dl*-mannonic acid). It is identical with the synthetically prepared α-*acritol* (from α-acrose, p. 699) (Ber. **23**, 383). It resembles ordinary mannitol, but in aqueous solution is inactive even in the presence of borax. Nitric acid oxidizes it to inactive mannose and inactive mannonic acid. The latter can be resolved into *d*- and *l*-mannonic acids (Ber. **23**, 392). *d*- and *l*-Mannonolactones may be reduced to *d*- and *l*-mannoses, and these to *d*- and *l*-mannitols. All of these compounds have been synthesized in this way.

2. *d*- and *l*-**Iditols** are colourless syrups formed by the reduction of *d*- and *l*-idoses ; *tribenzal* compounds, m.p. 219–223° (Ber. **28**, 1979).

3. *d*-**Sorbitol** (configuration, p. 705), $CH_2OH(CHOH)_4CH_2OH + H_2O$, m.p. 75° (anhydrous, 104–109°), occurs in mountain-ash berries, forming small crystals which dissolve readily in water. It is produced in the reduction of *d*-dextrose, and together with *d*-mannitol in the reduction of *d*-fructose (p. 698) (Ber. **23**, 2623). It is reduced to secondary hexyl iodide (Ber. **22**, 1048) when heated with hydriodic acid.

Sorbitol triformal, $C_6H_8O_6(CH_2)_3$, m.p. 206° (Ann. **289**, 23).

Triacetone sorbitol, $C_6H_8O_6(C_3H_6)_3$, m.p. 45°, b.p. 172°/25 mm.

l-**Sorbitol**, m.p. 75°, is obtained by the reduction of *l*-gulose (p. 696) Ber. **24**, 2144).

4. **Dulcitol**, *melampyrin*, $CH_2OH(CHOH)_4CH_2OH$ (configuration, p. 705), m.p. 188°, occurs in various plants, and is obtained from dulcitol manna (originating in Madagascar). It is produced artificially by the action of sodium amalgam on *d*-galactose. It crystallizes in large monoclinic prisms, having a sweet taste. It dissolves in water with more difficulty than mannitol, and is almost insoluble even in boiling water. Its solution remains optically inactive even in the presence of borax (Ber. **25**, 2564). Hydriodic acid converts it into the same hexyl iodide

that mannitol yields. Nitric acid oxidizes dulcitol to mucic acid. (Ber. **20**, 1091).

Hexaacetyl dulcitol, m.p. 171°.

Dimethylene dulcitol, $C_6H_{10}O_6(CH_2)_2$, m.p. 244° (Ann. **299**, 318). *Dibenzal dulcitol*, $C_6H_{10}O_6(CHC_6H_5)_2$, m.p. 215–220° (Ber. **27**, 1554). *Diacetone dulcitol*, $C_6H_{10}O_6(C_3H_6)_2$, m.p. 98°, b.p. 194°/18 mm. (Ber. **28**, 2533). *Dulcitol hexanitrate*, m.p. about 95°. *Dulcitol pentanitrate*, m.p. about 75° (Ber. **36**, 799).

5. ***d*-Talitol**, m.p. 86°, is produced in the reduction of *d*-talose.

Tribenzal-d-*talitol*, m.p. 206° (Ber. **27**, 1527 : C. 1908, I. 1529).

***dl*-Talitol**, m.p. 66°, is formed by the reduction of the body produced when dulcitol is oxidized with PbO_2 and hydrochloric acid (Ber. **27**, 1530).

6. **Rhamnohexitol**, $CH_3{\cdot}[CHOH]_5{\cdot}CH_2OH$, m.p. 173°, is formed when rhamnohexose (p. 698) is reduced with sodium amalgam (Ber. **23**, 3106).

7. **Glucamines.**—These bodies stand in the same relation to the hexose imines and amines (p. 699) as the hexitols to the hexoses. They are formed (1) from the hexose oximes, and (2) the hexoseamines by reduction with sodium amalgam.

d-*Glucamine*, $CH_2OH{\cdot}[CHOH]_4CHNH_2$, m.p. 128°, is prepared from dextrose oxime and also from *iso*dextrosamine (p. 700). It is a strong base, and is dextrorotatory. Together with the above is formed d-*mannamine*, m.p. 139°.

d-*Galactamine*, m.p. 139°, is lævorotatory (C. 1902, II. 1356 : 1903, II. 1237 : 1904, I. 871).

1 B. HEPTAHYDRIC ALCOHOLS

Perseitol or *mannoheptitol*, $C_7H_9(OH)_7$, is known in three modifications: d-*mannoheptitol*, m.p. 187°, l-*mannoheptitol*, m.p. 187°, and dl-*mannoheptitol*, m.p. 203°. *d*-Mannoheptitol or perseitol occurs in *Laurus persea*, and is obtained, like the other two modifications, by the reduction of the corresponding mannoheptoses (Ber. **23**, 936, 2231). *dl*-Mannoheptitol is formed when equal quantities of *d*- and *l*-mannoheptitol are mixed (Ann. **272**, 189). Hydriodic acid reduces it to hexahydrotoluene (Ber. **25**, R. 503).

α-Glucoheptitol, $CH_2OH(CHOH)_5CH_2OH$, m.p. 128°, is obtained from α-glucoheptose (p. 700 : Ann. **270**, 81). *Triacetone-α-glucoheptitol*, $C_2H_{10}O_7(C_3H_6)_3$, b.p. 200°/24 mm. (Ber. **28**, 2534).

α-Galaheptitol, $C_7H_{16}O_2$, m.p. 183°, is obtained from α-galaheptose (p. 700).

Volemitol, $C_7H_9(OH)_7$, m.p. 156°, dextrorotatory, is found in the pileated mushroom, *Lactarius volemus* (Ber. **28**, 1973), and in the *Primulaceæ* (C. 1902, II. 1513).

Anhydro-nonaheptitol, $C_9H_{16}O_5$, m.p. 156°, is formed from acetone and formaldehyde with lime and water. It is an anhydride of the heptahydric alcohol $[CH_2OH]_3 \colon C{\cdot}CH(OH)C \colon [CH_2OH]_3$ (Ber. **27**, 1089 : Ann. **289**, 46).

1 C. OCTAHYDRIC ALCOHOLS

α-Glucooctitol, $CH_2OH[CHOH]_6{\cdot}CH_2{\cdot}OH$, m.p. 141°, is obtained from α-glucooctose (p. 700 : Ann. **270**, 98).

***d*-Mannooctitol**, $CH_2OH[CHOH]_6CH_2OH$, is produced from mannooctose, m.p. 258°. It dissolves with difficulty in water.

1 D. NONOHYDRIC ALCOHOL

Glucononitol, $C_9H_{20}O_9$, m.p. 194°, is obtained from gluconpředose (Ann. **270**, 107).

2 and 3. PENTA-, HEXA-, HEPTA-, AND OCTO-HYDROXYALDEHYDES AND KETONES

The long-known representatives of the first class of carbohydrates, which are produced by hydrolysis from the more complex carbohydrates, the disaccharides (p. 721), like sucrose, maltose, and lactose, and from the polysaccharides,—*e.g.* starch, dextrin, cellulose, and others,—are pentahydroxyaldehydes and pentahydroxyketones.

The most important sugar of the first class is glucose, formed together with fructose by the hydrolysis of sucrose. It also occurs as the final product of the hydrolysis of starch and of dextrin. Glucose and fructose have already been referred to with ethyl alcohol, in connection with its formation by alcoholic fermentation (p. 140).

The aldehyde character of these bodies is inferred from the ready oxidation of certain dextroses to monocarboxylic acids, and their reduction to hexahydric alcohols. *Zincke* (1880) was the first (Ber. **13,** 641 Anm.) to suspect that ketone alcohols were represented among the hexoses. *Kiliani*, in 1885, investigating the HCN addition products, proved that glucose must be regarded as an aldehyde alcohol, and fructose as a ketone alcohol. Hence, it is customary to distinguish *aldoses* and *ketoses*. The same chemist also showed that arabinose was an aldopentose, and in so doing laid the basis of an extension of the idea of carbohydrates. What was lacking was a method of synthesis. Sugar-like bodies had already been obtained from formaldehyde (p. 235), but *Emil Fischer* first demonstrated that a well-defined sugar, *α-acrose*, could be isolated from it. This, as will be observed later, became in his hands the starting-point for the synthesis of glucose and of fructose.

By reducing the lactones of the polyhydroxycarboxylic acids to hydroxyaldehydes or aldoses, Fischer developed a method for the preparation of higher hydroxyaldehydes from the polyhydroxycarboxylic acids obtained synthetically from aldoses by the addition of hydrocyanic acid and subsequent hydrolysis. In this way carbohydrates, containing seven, eight, and nine carbon atoms in the molecule, were gradually built up (p. 700).

The hexoses mostly crystallize badly, and for their isolation and recognition phenylhydrazine and its derivatives were used. This, Fischer also discovered, gave the very best assistance. *Wohl* showed how the oximes of the aldoses could be utilized for their degradation (p. 673).

The monose character of a compound is due to its constitution, as an aldehyde alcohol, $—CH(OH)\cdot CHO$, or a ketone alcohol, $—CO\cdot CH_2\cdot OH$, in which the aldehyde and ketone group is directly combined with an alcohol group or groups. We thus have monoses containing not only six, but also a less or greater number of carbon and oxygen atoms. They are named according to the number of the oxygen atoms.

The simplest aldose, glycolyl aldehyde, $CH_2OH\cdot CHO$, is an *aldodiose*. Glyceric aldehyde, $CH_2OH\cdot CHOH\cdot CHO$, and dihydroxyacetone, $CH_2OH\cdot CO\cdot CH_2OH$, represent an *aldotriose* and a *ketotriose* (p. 589). The aldehyde and ketone of erythritol are *aldo-* and *keto-tetroses*, as just developed under the pentoses (p. 650). Following the latter are the hexoses. In this class belong the real sugars: *glucose*, *fructose*, and *galactose*.

In addition to the long-known hexoses—glucose, fructose, and galactose—many others have been discovered through Fischer's investigations. The hexoses will be considered in immediate connection with their corresponding hexahydric alcohols. Then follow the heptoses, octoses, and nonoses, as well as the oxidation products of these aldehyde and ketone alcohols : the polyhydroxymonocarboxylic acids, the polyhydroxyaldehydrocarboxylic acids, and the polyhydroxypolycarboxylic acids. After the consideration of all these, the higher carbohydrates, the disaccharides, and the polysaccharides, which are the anhydrides of the hexoses, will be brought together and fully discussed (p. 721).

2 A. PENTAHYDROXYALDEHYDES AND 3 A. PENTAHYDROXYKETONES : HEXOSES, MONOSES

References : Preparation, properties and derivatives of hexoses, see *Abderhalden*, Handbuch der biologischen Arbeitsmethoden, Lfgen. 52, 72, 83 : *G. Zemplen*, Kohlenhydrate : *H. Pringsheim*, Zuckerchemie, 1925 : *W. N. Haworth*, Constitution of sugars, London, 1929 : *E. F.* and *K. F. Armstrong*, Glycosides, London, 1931 : Constitutional investigation between 1923 and 1926, see *J. Leibowitz*, Z. angew. Chem. **1926**, 1143, 1240.

Occurrence.—Some hexoses occur widely distributed in the free state in the vegetable kingdom, especially in ripe fruits. Esters of the glucoses (from γλυχυς, sweet) with organic acids are also frequently found in plants. They are called *glucosides**—*e.g.* salicin, amygdalin, coniferin, the tannins, which are dextrose esters of the tannic acids, etc. The glucosides are split into their components by ferments, acids, or alkalis.

Formations.—(1) They are formed by the hydrolytic decomposition of all di- and poly-saccharides, as well as of glucosides, by ferments (p. 755) (Ber. 28, 1429), or by boiling them with dilute acids. (2) *d*-Mannose and *d*-fructose have been made artificially by oxidizing *d*-mannitol. (3) A far more important method pursued in the formation of the dextroses is to reduce the monocarboxylic lactones with sodium amalgam in acid solution (*Fischer*, Ber. 23, 930). (4) Different optically inactive hexoses, particularly α-acrose or *dl*-fructose (p. 699), have been directly synthesized by the condensation of formic aldehyde, CH_2O, and glyceric aldehyde.

The *dl*-fructose, prepared in this way by Fischer, is the parent substance for the complete synthesis of the naturally occurring mannitol, glucose and fructose.

Properties.—The hexoses are mostly crystalline substances, very soluble in water, but dissolving with difficulty in alcohol. They possess a sweet taste. The representatives of the hexoses occurring in nature rotate the plane of polarization, when in solution, either to the left or to the right. The stereoisomers of the more important hexoses found in nature have been prepared artificially, and by the union of the corresponding dextro- and lævo-forms the optically inactive *dl*-varieties have been obtained. One of these, *dl*-fructose or α-acrose, as previously mentioned, has been directly synthesized.

Reactions.—The hexoses show the general reactions of the alcohols, the aldehydes, and the ketones.

(1) The alcoholic hydrogen of the hexoses can also be replaced by metals on treating them with CaO, BaO, and PbO, forming *saccharates*, which correspond with the alcoholates, and which are decomposed by carbon dioxide.

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* See footnote on p. 672.

(2) On treating the alcoholic solutions of the hexoses with a little gaseous hydrochloric acid, their ethers result: *glucosides* of the alcohols (Ber. **26,** 2400 : **29,** 2927) (see p. 689).

(3) The hexoses combine with aldehydes, particularly with chloral, and with ketones, in the presence of inorganic acids, with an accompanying loss of water (Ber. **28,** 2496).

(4*a*) The hydrogen of the hydroxyls can be readily replaced by acid radicals. A mixture of nitric and sulphuric acids (p. 373) converts them into esters of nitric acid (Ber. **31,** 73)—so-called nitro-compounds (p. 583). The acetyl esters are best obtained by heating the sugars with acetic anhydride and sodium acetate or $ZnCl_2$, whereby five acetyl groups are thus introduced (Ber. **22,** 2207). The pentabenzoyl esters are prepared with even less difficulty, it being only necessary to shake the hexoses with benzoyl chloride and sodium hydroxide (p. 374) (Ber. **22,** R. 668 : **24,** R. 791).

The esters of *p*-toluenesulphonic acid are very readily obtained by the action of *p*-toluenesulphonyl chloride on the hexoses. The hexosephosphoric esters (p. 695) are of great importance as components of the nucleic acids (p. 748) and as intermediate compounds in alcoholic fermentation (p. 140).

Estimation of the entering acyl groups, see Ber. **12,** 1531 : Ann. **220,** 217 : Ber. 23, 1442.

(4*b*) The action of silver oxide and methyl iodide, or of dimethyl sulphate and alkali on the hexoses, or on the glucosides referred to above (2), leads to the formation of methyl ethers of these compounds.

5. The action of chlorosulphonic acid leads to the formation, as in the case of the monohydric alcohols, to the formation of alkylsulphuric acids (Ber. **17,** 2457) : similarly, by the action of chloroformic ester in absolute pyridine, one or more carbalkoxy-groups can be introduced (J.C.S. **1926,** 1751).

6. Like other hydroxy compounds, the hexoses react with phenyl *iso*cyanate to produce phenylurethanes (Ber. **18,** 2606 : C. 1904, I. 1068).

The following reactions depend upon the aldehyde and ketonic character of the hexoses :—

1. On *reduction* they yield the corresponding hexahydric alcohols, *e.g.* *d*-mannose and *d*-fructose yield *d*-mannitol, with some *d*-sorbitol, galactose yields dulcitol, and glucose sorbitol, with some mannitol.

2. The *oxidation* of the hexoses is readily brought about by mild oxidizing agents, and the hexoses therefore behave as mild reducing substances.

They reduce the salts of the noble metals, with precipitation of the metal, and reduce ammoniacal silver solutions in the cold. Their property of reducing alkaline copper solutions with the precipitation of cuprous oxide is characteristic, and is made use of in their detection and estimation. One molecule of glucose precipitates approximately five atoms of copper as Cu_2O. *Fehling's solution*, prepared from copper sulphate, sodium potassium tartrate (Rochelle salt) and sodium hydroxide is frequently used for the purpose, but *Benedict's solution*, prepared from copper sulphate, sodium citrate and sodium carbonate has certain advantages. It is less alkaline than Fehling's solution, and is therefore less likely to destroy small amounts of sugar, and is also rather less easily reduced by certain other substances such as uric acid and creatinine which occur in urine. The oxidation-products of the hexoses formed by the action of Fehling's solution varies according to the concentration, and consist partly of penta-hydroxycarboxylic acids (p. 711) and partly of acids of lower carbon content down to formic and carbonic acids (Ann. **357**, 259).

The hexoses are converted into their corresponding monocarboxylic acids (p. 711) by moderated oxidation with chlorine and bromine water, or silver oxide. The ketoses are more stable than the aldoses towards bromine and iodine solutions (see p. 694).

More energetic oxidation changes them to saccharic or mucic acids.

(3) The aldohexoses in concentrated solution produce a red coloration in a sulphite-fuchsine solution (*Schiff's* reagent). The penta-acetyl and pentabenzoyl derivatives of the hexoses no longer show this aldehyde reaction (Ber. **21**, 2842 : **22**, R. 669).

(4) The aldoses yield mercaptals with mercaptans, in the presence of hydrochloric acid (Ber. **27**, 673).

(5) *Oximes* are produced when alcoholic hydroxylamine acts on the hexoses. To break down the aldoses, the acetyl hydroxy-acid nitriles, obtained from the aldoximes and acetic anhydride, are split into hydrocyanic acid and acetyl pentoses (p. 673) (Ber. **24**, 993 : **26**, 730). This reaction has more recently been employed in a modified form for the degradation of the reducing disaccharides (Ber. **59**, 1254).

(6*a*) Osamines are formed when the hexoses are acted on with methyl alcoholic ammonia.

(6*b*) The hexoses and aniline, as well as its homologues, yield the anilides—*e.g.* dextrose anilide, $CH_2OH[CHOH]_4CH : NC_6H_5$, which form cyanides with HNC —*e.g.* anilidodextrose cyanide, $CH_2OH[CHOH]_4{\cdot}CH{\cdot}(CN)NHC_6H_5$ (Ber. **27**, 1287).

(7) Hydrazine converts the aldohexoses into aldazines, and the ketohexoses into ketazines (p. 693) (Ber. **29**, 2308).

(8) The compounds formed with phenylhydrazine and its derivatives are especially important.

(*a*) If one molecule of the hydrazine, as acetate, is allowed to act, the first product will be a hydrazone, $C_6H_{12}O_5{\cdot}(N{\cdot}NH{\cdot}C_6H_5)$. This class of compounds dissolves readily in water (with the exception of those derived from mannose and some disaccharides, Ber. **23**, 2118). They generally crystallize from hot alcohol in colourless needles. Cold concentrated hydrochloric acid resolves them into their components. Benzaldehyde is also an excellent reagent for the decomposition of the phenylhydrazones (Ann. **288**, 140).

With *as.*-diphenylhydrazine the slightly soluble diphenylhydrazones are mainly formed (Ber. **23**, 2619, etc.). Benzylphenylhydrazine is very well suited for the preparation of pure sugars : the benzylphenylhydrazones are decomposed by formaldehyde, whereby the sugar is liberated and *formaldehyde benzylphenylhydrazone*, m.p. 41°, is formed (Ber. **32**, 3234). Also, *as.*-methylphenylhydrazine, bromophenylhydrazine, and β-naphthylhydrazine have been recommended from time to time for the precipitation and separation of the sugars (Ber. **35**, 4444, etc.).

(*b*) In the presence of an excess of phenylhydrazine the hexoses combine with two molecules of it upon application of heat and form the *osazones* (*E. Fischer*):

$$C_6H_{12}O_6 + 3H_2N{\cdot}NH{\cdot}C_6H_5 = \underset{\text{Glucosazone.}}{C_6H_{10}O_4(N{\cdot}NH{\cdot}C_6H_5)_2} + 2H_2O + C_6H_5{\cdot}NH_2 + NH_3.$$

In this reaction a hydrazone is first produced, and one of its alcohol groups, adjacent to either an aldehyde or ketone group, is oxidized to CO, two hydrogen atoms in the presence of excess of phenylhydrazine appearing as aniline and ammonia; the aldehydo- or keto-group, which is formed, reacts further on a second molecule of phenylhydrazine. One and the same *glucosazone*, $CH_2OH{\cdot}(CHOH)_3{\cdot}C(N_2HC_6H_5){\cdot}CH(N_2HC_6H_5)$ (Ber. **23**, 2118), is thus obtained from *d*-mannose, *d*-glucose, and *d*-fructose. This indicates that the four carbon atoms which do not react with phenylhydrazine have the same stereochemical configuration.

The reaction is carried out by adding three parts of phenylhydrazine, two parts of 50 per cent. acetic acid, and about twenty parts of water to one part of dextrose. This mixture is digested for about one hour upon the water bath. The osazone then separates in a crystalline form (Ber. **17**, 579: **20**, 821: **23**, 2117).

It is of importance in the separation of aldoses and ketoses that with *as.*-alkyl phenylhydrazines, such as α-methylphenylhydrazine, only the ketoses yield the yellow *methylphenylosazones*, whilst the aldoses give the simple colourless hydrazones (Ber. **35**, 959, 2626).

The osazones are yellow-coloured compounds (see Tartrazine, p. 663). They are usually insoluble in water, dissolve with difficulty in alcohol, and crystallize quite readily. When glucosazone is reduced with zinc dust and acetic acid it becomes converted into *iso*glucosamine (p. 700). Nitrous acid converts the latter into lævulose (Ber. **23**, 2110). The re-formation of the hexoses from their osazones is readily effected by digestion with concentrated hydrochloric acid; they are then resolved into phenylhydrazine and the *osones* (Ber. **22**, 88: **23**, 2120: **35**, 3141):

$$\underset{\text{Glucosazone.}}{C_6H_{10}O_4(N_2H{\cdot}C_6H_5)_2} + 2H_2O = \underset{\text{Glucosone.}}{CH_2OH{\cdot}(CHOH)_3{\cdot}CO{\cdot}CHO} + 2N_2H_3{\cdot}C_6H_5.$$

The osones dissolve readily in water, and have not been obtained pure. They are also formed from aldoses and ketoses directly by oxidation with H_2O_2 in presence of ferrous salts (C. 1902, I. 859). They combine, like keto-aldehydes, with two molecules of phenylhydrazine and form osazones. They are converted into ketoses by reduction, as when digested with zinc dust and acetic acid. In this way fructose is obtained from glucosazone (Ber. **23**, 2121).

The osones, like all orthodicarbonyl compounds, yield quinoxalines (Ber. **23**, 2121) with the *o*-diamines. The hexoses also combine directly with the *o*-phenylenediamines (Ber. **20**, 281).

Synthetic and Degradation Reactions of the Hexoses.

(1) *Synthesis.*—Being aldehydes or ketones, the hexoses combine with hydrocyanic acid, forming cyanohydrins, which yield monocarboxylic acids (p. 715). Their lactones can in turn be reduced to aldoses by means of sodium amalgam, whereby the synthesis of the next higher monose is achieved. Usually in the hydrogen cyanide addition the nitriles of both the acids possible theoretically are produced, but not in equal amounts.

These two reactions make possible the genetic connection of the following aldoses (Ber. **27**, 3192):

$$\begin{tikzcd}
& \text{\textit{l}-Mannose} \arrow[r] & \text{\textit{l}-Mannoheptose} & \\
\text{\textit{l}-Arabinose} \arrow[ur] \arrow[dr] & & & \\
& \text{\textit{l}-Glucose} & & \\
& \text{\textit{l}-Idose} & & \\
\text{\textit{l}-Xylose} \arrow[ur] \arrow[dr] & & & \\
& \text{\textit{l}-Gulose} & & \\
\text{Rhamnose} \arrow[r] & \text{\textit{d}-Rhamnohexose} \arrow[r] & \text{Rhamnoheptose} \arrow[r] & \text{Rhamno-octose} \\
\text{\textit{d}-Mannose} \arrow[r] & \text{\textit{d}-Mannoheptose} \arrow[r] & \text{\textit{d}-Manno-octose} \arrow[r] & \text{\textit{d}-Mannononose} \\
& & \alpha\text{-Gluco-octose} \arrow[r] & \text{Gluconononose} \\
& \alpha\text{-Glucoheptose} \arrow[ur] \arrow[dr] & & \\
\text{\textit{d}-Dextrose} \arrow[ur] \arrow[dr] & & \beta\text{-Gluco-octose} & \\
& \beta\text{-Glucoheptose} & & \\
& \alpha\text{-Galaheptose} \arrow[r] & \text{Galaoctose} & \\
\text{\textit{d}-Galactose} \arrow[ur] \arrow[dr] & & & \\
& \beta\text{-Galaheptose} & &
\end{tikzcd}$$

2. The *degradation* of the aldohexoses to the aldopentoses, either through their oximes (*Wohl*) or by the action of hydrogen peroxide on the gluconic acids, has already been discussed (p. 673). The degradation can also be brought about by the action of sodium hypochlorite on the amides of the monocarboxylic acids (Rec. Trav. Chim. **37**, 16). A modified method has been used for the degradation of the reducing disaccharides (p. 723: *Zemplén*, Ber. **59**, 1254).

(3) The behaviour of the hexoses with *alkalis*, such as the hydroxides of sodium, calcium, lead, zinc, etc., is noteworthy. Dilute alkalis strongly depress the optical rotation of the naturally occurring hexoses, as a result of partial isomerization to the stereomeric aldoses and ketoses as far as the point of equilibrium (see Ber. **28**, 3078: Ann. **357**, 294). Mannose, glucose, and fructose yield a mixture of these three hexoses, together with ψ-lævulose and glutose (or 3-ketohexose ?); similarly, galactose may yield *l*-sorbose, *d*-tagatose, talose, and galtose (or 3-ketohexose ?).

Longer action of alkalis decomposes this mixture of hexoses mainly into lactic and other acid (Ber. **41**, 1009). It is probable that the formation of lactic acid results from the initial formation of glyceraldehyde, which loses oxygen and is changed into methylglyoxal (p. 400), which in turn changes into lactic acid:

$$\begin{array}{l}
CH_2(OH)CH(OH)CH(OH) \\
\qquad\qquad\qquad\quad | \\
\underset{\text{3-Ketohexose (see above).}}{CH_2(OH)CH(OH)CO} \longrightarrow \underset{\text{Glyceraldehyde.}}{2CH_2(OH)CH(OH)\cdot CHO} \longrightarrow \\
\qquad\qquad\qquad\qquad\qquad \underset{\text{Methylglyoxal.}}{2CH_3CO\cdot CHO} \longrightarrow \underset{\text{Lactic acid.}}{2CH_3CH(OH)COOH}
\end{array}$$

The formation of methylglyoxal, according to the above scheme, is made the more probable by the action of zinc ammonium hydroxide on dextrose, producing methylglyoxaline, which is presumably formed from methylglyoxal and ammonia (p. 399) (Ber. **39**, 3886).

The formation of methylglyoxal in muscle and its immediate dismutation into lactic acid is discussed in Z. physiol. Chem. **161**, 254.

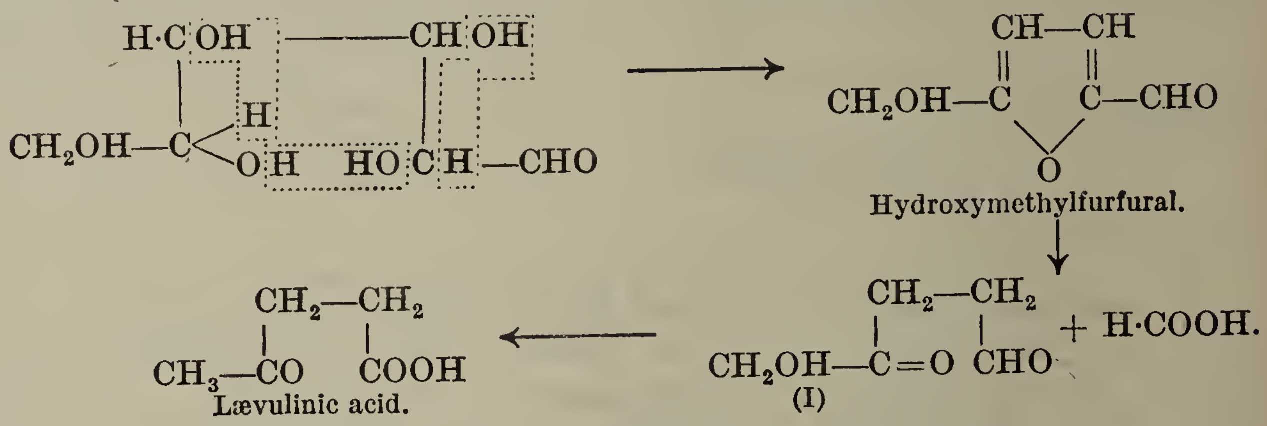
In addition to the products of reaction between hexoses and alkalis, there are also formed—particularly when lime-water is employed—*saccharic acids* (p. 676), the production of which results partly from an intra-molecular wandering of oxygen, and also in a change of the form of the normal carbon chain (*cf.* Ann. **357**, 294: Ber. **41**, 469, 1012).

If air be passed through an alkaline solution of the hexoses, or if H_2O_2 be added, formic acid is formed, together with higher non-volatile acids: the production of the former acid is explained by partial decomposition of the hexose into formaldehyde and the oxidation of the latter into its acid (Ber. **39**, 4217) (see also p. 684: *Fehling's solution*).

4. All hexoses are converted on heating with concentrated sulphuric acid into lævulinic acid, whereby they are sharply differentiated

from the pentoses, which under similar treatment yield furfural (see p. 672).

The mechanism of the formation of lævulinic acid is explained by Pummerer (Ber. **56**, 999) on the basis of the behaviour of furfuralcohol. The first intermediate is the compound hydroxymethylfurfural (Chem. Ztg. **1895, 1004**) which on opening the ring loses formic acid and forms the hydroxyketoaldehyde (I) which undergoes intramolecular change with the formation of lævulinic acid :



5. *Fermentation of the Hexoses.*—A characteristic of the hexoses is their ability to ferment with the production of various compounds by the action of yeasts, moulds and bacteria. The more important fermentations are mentioned below : for further information consult *Harden* in *System of Bacteriology*, I. 217 (London, 1929) : *Raistrick*, *Phil. Trans.* 1931, [B] **220**, 1–367 (Moulds) :

(*a*) *Alcoholic fermentation* of hexoses, which is brought about by yeasts, is the most important of these processes, and has been discussed on p. 140. Of the aldoses, *d*-glucose, *d*-mannose and *d*-galactose and of the ketoses *d*-fructose are fermented. The other hexoses are not attacked by yeast (Ber. **27**, 2030).

(*b*) *Lactic acid fermentation* of various carbohydrates, which can be represented by the equation :

$$C_6H_{12}O_6 \longrightarrow 2C_3H_6O_3$$

is brought about by a large number of organisms. It is probably due to the intermediate formation of methylglyoxal (see under alcoholic fermentation, p. 140), which then undergoes dismutation by the enzyme glyoxalase to lactic acid. In some cases lactic acid is formed in almost quantitative yield : the acid produced is usually the inactive *dl*-acid, but some organisms, *e.g. B. delbrücki*, produce an optically active *l*-lactic acid. In other cases, the yield of lactic acid is not quantitative, but other compounds are formed. For instance, with *B. coli* and *B. typhosus* formic acid is also produced, but whereas with the former organism this is largely broken down into CO_2 and hydrogen, the latter organism is incapable of doing this and formic acid accumulates in the medium.

The property of forming acid and/or gas in culture media containing various carbohydrates is made practical use of in the classification of certain groups of bacteria.

Another compound formed along with lactic acid by certain organisms, *e.g. B. lactis aerogenes*, is *βγ*-butylene glycol, a certain amount of acetylmethylcarbinol, $CH_3{\cdot}CO{\cdot}CH(OH){\cdot}CH_3$, being simultaneously produced. The formation of the ketone is due to the condensation of two molecules of acetaldehyde under the action of the enzyme *carboligase*, the glycol being formed by reduction :

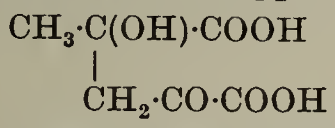
$$CH_3{\cdot}CHO + CHO{\cdot}CH_3 \longrightarrow CH_3{\cdot}CH(OH){\cdot}CO{\cdot}CH_3.$$

(*c*) *Propionic Acid Fermentation.*—Micro-organisms occur in milk and cheese which have the property of producing a mixture of propionic (2 mols.) and acetic (1 mol.) acids together with CO_2, from certain hexoses, and also from other compounds such as lactic acid and glycerol. The mechanism of this mode of fermentation is not quite settled ; according to Virtanen a phosphoric ester of the sugar is produced, which then forms lactic acid, the latter breaking down according to the equation:

$$3C_3H_6O_3 \xrightarrow{\qquad} 2C_3H_6O_2 + C_2H_4O_2 + CO_2 + H_2O,$$

but according to van Niel methylglyoxal is the intermediate.

(*d*) *Butyric Fermentation.*—Another group of organisms has the power of forming butyric acid or butyl alcohol from substrates such as glucose or glycerol. Thus *B. butylicus*, Fitz. produced 26% of butyric acid from glucose, and 19·6% of butyl alcohol from glycerol. It would appear that the aldol of pyruvic acid:



$$\begin{array}{l}\mathrm{CH_3{\cdot}C(OH){\cdot}COOH}\\ \qquad\quad |\\ \qquad\;\mathrm{CH_2{\cdot}CO{\cdot}COOH}\end{array}$$

is the intermediate product. Higher homologues of butyric acid are also obtained in small yield.

Another group of organisms, *B. amylobacter*, has the property of fermenting starch with the formation of large amounts of butyl alcohol and acetone, and this process is used on the large scale for the manufacture of these solvents.

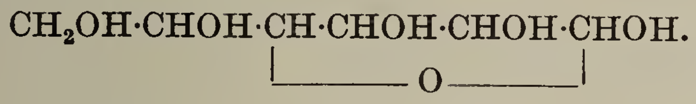
(*e*) *Citric acid* is obtained by the fermentation of glucose by certain fungi (see p. 664).

Constitution of the Hexoses

The reactions already described offered evidence that in the hexoses there was an unbranched chain of six carbon atoms (reduction to *n*-hexyl iodide) which contained five hydroxyl groups (formation of pentaacetyl derivative) and an aldehyde group (reaction with phenylhydrazine and hydroxylamine), and these reactions suggested the formula (I) which for a long time was used to represent the aldohexoses.

$$\mathrm{CH_2OH{\cdot}CHOH{\cdot}CHOH{\cdot}CHOH{\cdot}CHOH{\cdot}CHO.} \quad \text{(I)}$$

Further investigation, however, showed that this formula was not in entire agreement with all the experimental facts. Tollens, in 1883, had already noted the fact that the hexoses in ordinary concentrations did not redden a fuchsin-sulphurous acid solution (*cf.* E. Fischer, Ber. **45, 461**, note) and explained this discrepancy by a ring formula (II), isomeric with the above.



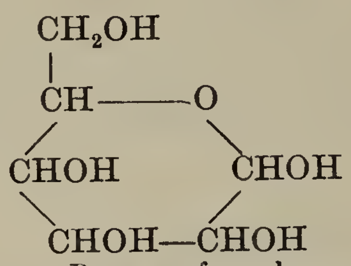
(II)

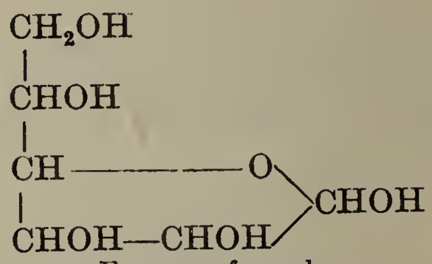
$$\mathrm{CH_2OH{\cdot}CHOH{\cdot}\underbrace{CH{\cdot}CHOH{\cdot}CHOH{\cdot}CHOH}_{O}.}$$

Subsequent investigations have confirmed the idea that in the hexoses there exists no normal aldehyde group: thus the reaction of Angeli with dihydroxyammonia (see p. 230) which is a typical aldehyde reaction, does not occur: investigations with simpler compounds shows that this reaction does not occur with hydroxyaldehydes containing the hydroxyl group in the γ- or δ-position relative to the aldehyde group.

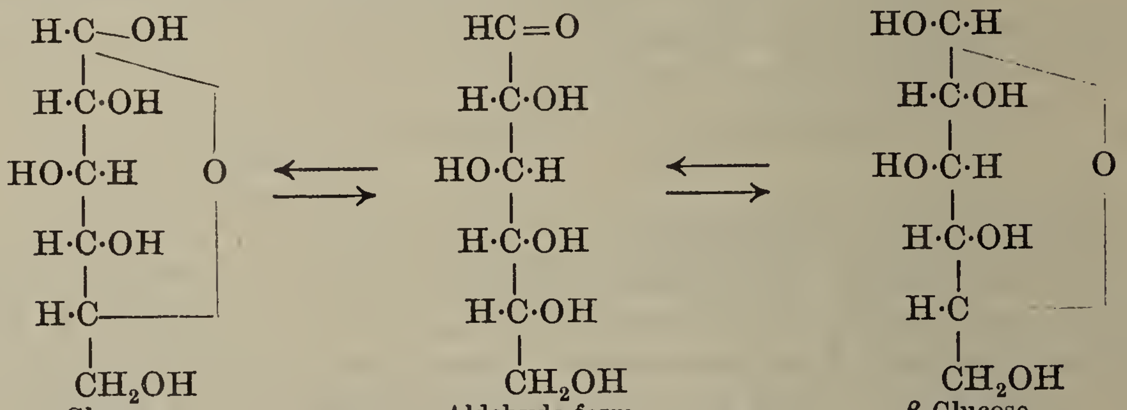
The formation of *glucosides* also differentiates the hexoses sharply from the aldehydes. In contradistinction to the latter, the hexoses form *semi-acetals* (only one alkyl group is introduced) when hydrogen chloride is led into an alcoholic solution. This is explained by assuming that the second valency of the aldehyde oxygen atom is engaged in an internal oxide ring, which explains at the same time the unique properties of the fifth hydroxyl group (the glucosidic hydroxyl).

The normal hexoses contain an amylene oxide (1 : 5 or 2 : 6) ring: less stable forms contain a butylene oxide (1 : 4 or 2 : 5) ring. For the latter labile isomer the designation *hetero*-sugar (*h*-glucose) (Ber. 58, 1842) is largely used in Germany: in the English-speaking countries the term γ-sugar is largely employed. This term originally applied to a third glucoside, derived from an isomeric sugar, which differed from the already known α- and β-glucosides. Fortuitously, the γ- in the light of more recent knowledge is also applicable to the γ- oxide ring which occurs in such sugars. More recently (Haworth) the designation *pyranose* (I) and *furanose* (II) has been suggested for the normal and labile forms, as they contain respectively a pyran (six-membered) carbon-oxygen ring and a furan (five-membered) ring. The terms pyranose and furanose will be chiefly used in the following pages.


Pyranose formula.

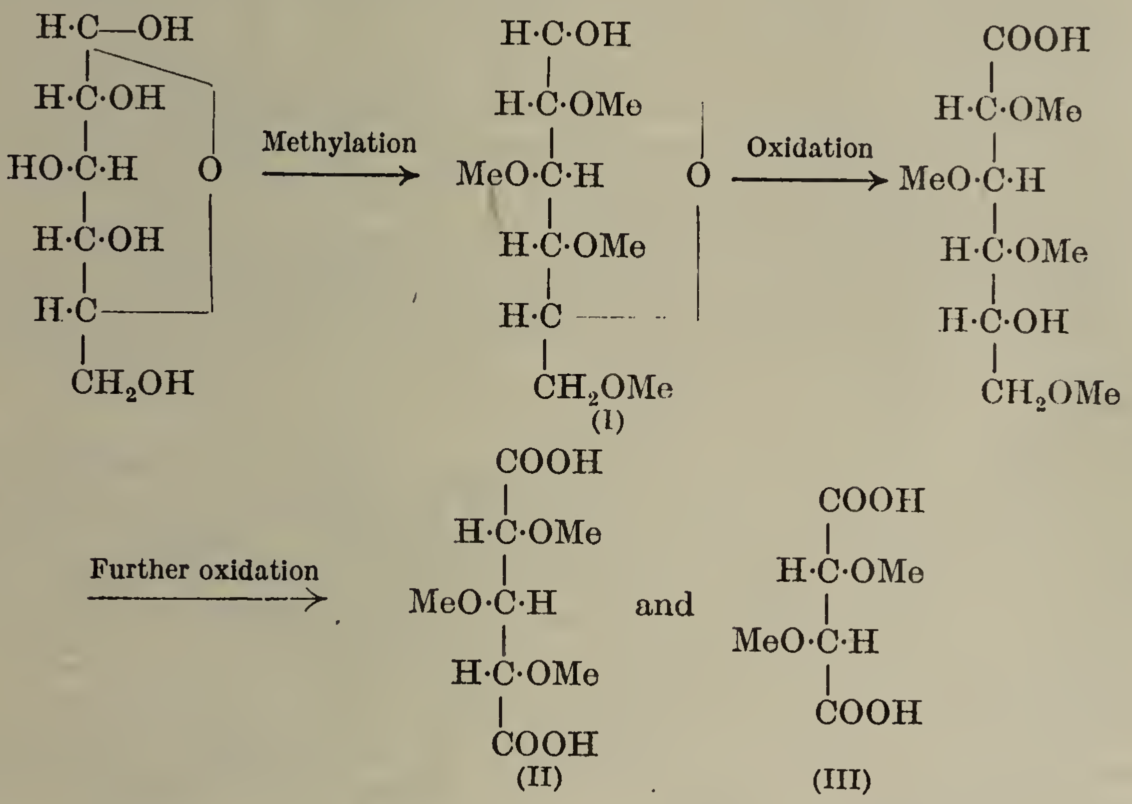

Furanose formula.

The ring formula for the hexoses, which contain an asymmetric carbon atom additional to those of the open aldehyde form, affords an explanation for the existence of two *d*-glucoses (α- and β-glucose), of the two methylglucosides and of two forms of pentaacetylglucose, and for the long-known phenomenon of mutarotation. This additional asymmetric carbon atom enables all hexoses to exist in two stereoisomeric forms (α- and β-series). These are capable of separate existence in the solid state, but in solution an equilibrium establishes itself with measurable speed between the α- and β-forms and the open aldehyde form, which can be demonstrated by a change of the optical activity of a solution with time (*Mutarotation*).


α-Glucose. Aldehyde form. β-Glucose.

The cyclic forms and the open aldehyde form are related to each other as tautomeric compounds (see p. 389). If the minute amount present of the aldehyde form is removed, as, for example, by means of phenylhydrazine, a fresh proportion of the aldehyde form is formed to restore equilibrium; this is then attacked by the reagent, and in effect the total amount of the hexose behaves as if it existed in the aldehyde form.

The experimental determination of the position of the internal oxygen linkage is of the greatest importance. The method is based on the stabilization of the alcoholic hydroxyl groups, by converting them into methoxy groups by one of the methods already described (p. 684). The tetramethylhexoses so obtained are converted by oxidation, through the tetramethylhexonic acids, to smaller molecules, from whose constitution the constitution of the original hexose can be calculated. The basis of this method is the assumption that under the conditions of experiment the position of the oxide ring is unchanged and there is no migration of any methyl group (J.C.S. **1927,** 3136). The following scheme represents the findings in the case of the most important hexose, *d*-glucose.



The energetic oxidation of ordinary tetramethylglucose (I) yielded inactive xylotrimethoxyglutaric acid (II) together with *d*-dimethoxysuccinic acid (III) whereby the 1 : 5-pyranose structure for normal glucose is deduced (Nature, **116,** 430 : J.C.S. **1926,** 350). Similar deductions form mannose, J.C.S. **1927,** 3136 : galactose, J.C.S. **123,** 1808 : **125,** 2468 : **127,** 348 : Ber. **59,** 100 : fructose, J.C.S. **1926,** 1858.

2 A. ALDOHEXOSES

(1) **Mannose,** $C_6H_{12}O_6$, is the aldehyde of mannitol, and exists in the three forms, *d*-, *l*- and *dl*-mannose, derived from the ordinary pyranose formula. Derivatives of the furanose sugar (1 : 4-oxide ring) are also known (J.C.S. **125,** 1343). Configuration of mannose, see p. 704. Evidence for 1 : 5-ring, see J.C.S. **1927,** 3136 : J. Biol. Chem. **72,** 627.

d-**Mannose,** *seminose,* m.p. 136°, was first prepared by oxidizing ordinary *d*-mannitol, together with *d*-fructose, with platinum black or nitric acid (Ber. **22,** 365). It is also obtained from salep mucilage (from salep, the tubers of certain orchids), and most easily from seminin (reserve-cellulose), occurring in different plant seeds, particularly in the shells of the vegetable ivory nut, when this is boiled with dilute sulphuric acid (hence called seminose) (Ber. **22,** 609, 3218).

d-Mannonic acid yields it upon reduction. It reduces Fehling's solution, and is fermented by yeast (Ber. **22**, 3223). When treated with alkalis it changes partly to *d*-glucose and *d*-fructose (p. 698).

Pentaacetyl-d-*mannose*, α-form, m.p. 75°, $[\alpha]_D$ + 55° ($CHCl_3$) (J. Biol. Chem. **72**, 627); β-form, m.p. 115°, $[\alpha]_D$ − 24·3° ($CHCl_3$) (Ber. **46**, 4029). The β-form is converted into the α- by anhydrous stannic chloride (Ber. **61**, 142). α-*Methyl*-d-*mannoside*, $C_6H_{11}O_6{\cdot}CH_3$, m.p. 190°, $[\alpha]^{20}_D$ + 79·2° (Ber. **29**, 2928 : **54**, 1567). *Pentanitrate*, m.p. 81° (Ber. **31**, 76). *Tetramethyl*-α-*methylmannoside*, m.p. 38°.

Phenylhydrazone, $C_6H_{12}O_5 : N{\cdot}NHC_6H_5$, m.p. 195°, is sparingly soluble in water, and regenerates, when treated with benzaldehyde, pure mannose (Ber. **29**, R. 913). The *osazone* is identical with glucosazone (*q.v.*). *Mannose oxime*, m.p. 184° (Ber. **24**, 699).

2 : 3 : 5 : 6-*Diacetonemannose*, m.p. 123°, $[\alpha]^{19}_{\text{Hg yellow}}$ + 14·3° (tetrachloroethane), is a derivative of γ-mannose (1 : 4-oxide ring) (Ber. **56**, 2125 : **58**, 2590).

Mannose is reduced by nascent hydrogen to mannitol, by oxidation with bromine converted into *d*-mannonic acid, and with hydrogen cyanide yields the nitrile of mannoheptonic acid (see p. 715).

l-**Mannose** results when *l*-mannonic lactone is reduced (p. 712 : Ber. **23**, 373). It is very similar to the preceding compound, but is lævorotatory, and is fermented with more difficulty. Its *phenylhydrazone*, m.p. 195°, also dissolves with difficulty. Excess of phenylhydrazine yields *l*-glucosazone. It becomes converted into *l*-mannitol by reduction (Ber. **23**, 375). *Methyl*-l-*mannoside*, m.p. 190°, $[\alpha]^{20}_D$ = − 79·4° (Ber. **29**, 2929).

dl-**Mannose** is formed (1) by the oxidation of α-acritol or *dl*-mannitol (p. 680), which can be obtained by the reduction of synthetic α-acrose or *dl*-fructose; (2) by the reduction of inactive *dl*-mannonic lactone; (3) by the splitting of a mixture of *d*- and *l*-mannose phenylhydrazones by formaldehyde (C. 1903, I. 1217). It is quite similar to the two preceding compounds, but is inactive. Its *phenylhydrazone*, m.p. 195°, dissolves with difficulty, and is inactive. Its *osazone* is *dl*-glucosazone, identical with α-acrosazone.

Yeast decomposes it, the *d*-mannose is fermented, and *l*-mannose remains (Ber. **23**, 382). *Methyl*-dl-*mannoside*, m.p. 165°, is obtained from the solution of equal quantities of its components at 15°. Below 8° the components crystallize out separately (Ber. **29**, 2929).

(2) **Glucose,** $C_6H_{12}O_6$, is the aldehyde of sorbitol, and occurs as *d*-, *l*-, and inactive *dl*-glucose.

d-Glucose, *dextrose*, or *grape sugar*, occurs (with fructose) in many sweet fruits and in honey; also in the urine in diabetes mellitus. It is normally present (about 0·1%) in blood, but its concentration in the blood is greatly increased in diabetes mellitus. It is formed by the hydrolytic decomposition of polysaccharides (sucrose, starch, cellulose) and glucosides. It is prepared on a large scale by boiling starch with dilute sulphuric acid (see Ber. **13**, 1761). The synthesis of glucose has been achieved by the production of glucose in the reduction of the lactone of *d*-gluconic acid (see p. 713).

Commercial dextrose is an amorphous, compact mass, containing only about 60% dextrose, along with a dextrin-like substance, *gallisin*, $C_{12}H_{24}O_{10}$, which is not fermentable (Ber. **17**, 2456).

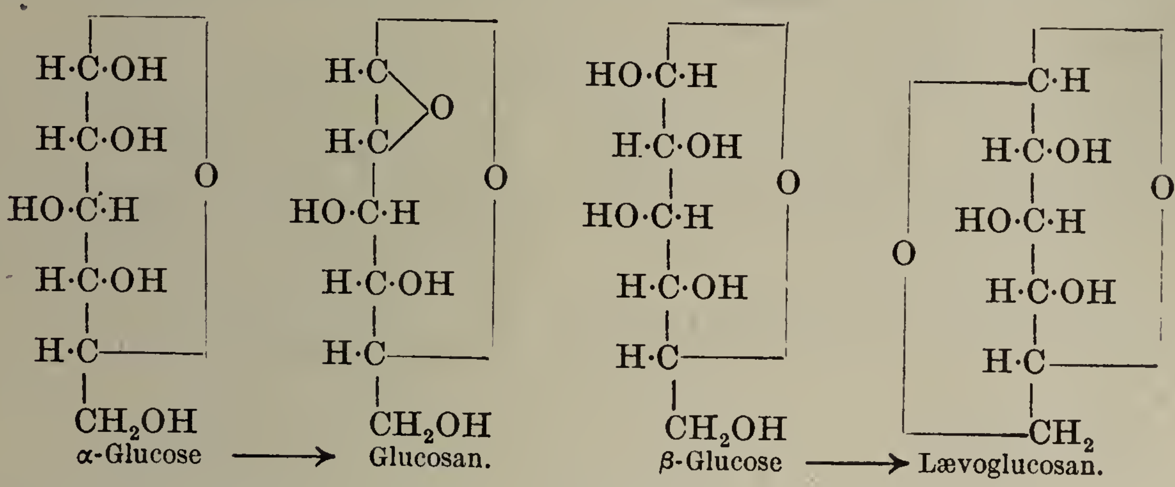
The best method for preparing pure crystallized glucose consists in adding to 80% alcohol mixed with $\frac{1}{15}$ volume of fuming hydrochloric acid, finely pulverized sucrose, as long as the latter dissolves on shaking (J. pr. Chem. [2] **20**, 244).

Glucose crystallizes from water at the ordinary temperature, or dilute alcohol, in nodular masses, with one molecule of water, which melt at 86° and become anhydrous at 115°. At 30–35° it crystallizes from its concentrated aqueous solution, and from its solution in ethyl or methyl alcohol, in anhydrous, hard crusts (Ber. **15**, 1105).

Dextrose is not quite as sweet to the taste as sucrose, and is employed to "improve" wines.

α- and *β-Glucose.*—Ordinary crystalline glucose is α-glucose and shows an initial rotation of $[\alpha]_D + 106°$ in aqueous solution. The specific rotation, however, falls on standing, and eventually reaches a constant value of + 53°, the solution now containing an equilibrium mixture of α- and β-glucose. Pure β-glucose has an initial specific rotation of + 19·8°, but its specific rotation rises to the same equilibrium value of 53° (*Mutarotation*). α-Glucose can be converted into the β-compound by heating in pyridine (Ann. **353**, 106) or glacial acetic acid (J.A.C.S. **39**, 329) solution, and can be obtained crystalline from such solutions under appropriate conditions.

The constitution of α- and β-glucose differs in the configuration of the 1- (aldehyde) carbon atom, as shown by the following reactions. α-Glucose gives on dehydration glucosan, whereas β-glucose gives lævoglucosan (see Ber. **46**, 2612: Helv. Chim. Acta. **3**, 649):



γ-Glucose (*Glucofuranose*).—A derivative of this sugar, with a 1 : 4-oxide ring, is *γ-methylglucoside* (Fischer, Ber. **47**, 1980: see p. 694).

Nitrogen derivatives of glucose. Syn- and anti- (α- and β-) d-*Glucose phenylhydrazones*, m.pp. 160° and 141°, are lævorotatory (Ann. **362**, 78).

d-*Glucosazone*, α-variety, m.p. 145°; β-variety, m.p. 205° (Ber. **41**, 75), is lævorotatory in aqueous solution. It is also obtained from *d*-mannose and *d*-fructose, as well as from glucosamine and *iso*glucosamine. Concentrated hydrochloric acid converts glucosazone into phenylhydrazine and glucosone, $C_6H_{10}O_6$ (p. 686); which regenerates glucosazone with two molecules of phenylhydrazine. It is a non-fermentable syrup (C. 1902, I. 895), and if it be reduced with zinc and acetic anhydride, is converted into *d*-fructose (Ber. **22**, 88).

d-*Glucoseoxime*, $C_6H_{12}O_5 : NOH$, m.p. 137°, by the action of acetic anhydride and sodium acetate yields pentaacetylgluconназвания nitrile (p. 713) from which arabinose has been isolated (p. 673). This action is the basis of Wohl's method for the degradation of the aldoses. Reduction to *d*-glucamine, see p. 681.

d-*Glucose semicarbazone*, m.p. 175° (decomp.) (Ber. **31**, 2199, note).

d-*Glucosealdazine*, $C_5H_{11}O_5{\cdot}CH : N{\cdot}N : CH{\cdot}C_5H_{11}O_5$, is very hygroscopic (Ber. **29**, 2308).

d-*Glucose aminoguanidine chloride*, $C_6H_{12}O_5{\cdot}CN_4H_4$, HCl, m.p. 165°, is obtained from glucose and aminoguanidine hydrochloride (Ber. **27**, 971).

Glucose is converted, by reduction with sodium amalgam, into *d*-sorbitol with some *d*-mannitol and by acid oxidation into *d*-gluconic acid and *d*-saccharic acid. Alkalis convert it partly into *d*-mannose and *d*-fructose (Ber. **28**, 3078) together with ψ-fructose and glutose (p. 687); prolonged action of alkalis produces lactic and other acid products (p. 687).

Milk of lime converts glucose partially into saccharinic acid (p. 676). Alkalis and benzhydrazide break up the glucose molecule, and form the benzoylosazone of glyoxal and methylglyoxal (Ber. **31**, 31). Ammonium zinc hydroxide gives methylglyoxaline (p. 399). For the products of alkaline oxidation of glucose, see pp. 684, 687, and Ber. **27**, R. 788.

Estimation of Glucose.—Many methods for the estimation of glucose are used, for details of which see textbooks of Biochemistry. A number of methods depend upon the reduction of an alkaline copper solution, the cuprous oxide formed being then estimated by various methods. The greater reactivity of aldoses towards an alkaline hypoiodite solution is made use of in the determination of glucose in presence of fructose by Willstätter and Schudel (Ber. **51**, 780).

Saccharates.—With barium and calcium hydroxide solutions dextrose forms saccharates, like $C_6H_{12}O_6{\cdot}CaO$, and $C_6H_{12}O_6{\cdot}BaO$, which are precipitated by alcohol. With NaCl it forms large crystals, $2C_6H_{12}O_6{\cdot}NaCl + H_2O$, which sometimes separate in the evaporation of diabetic urine.

Alkyl *d*-Glucosides.—The glucosides are the ether-like derivatives of the glucosidic hydroxyl group of the sugars. Those of dextrose particularly are frequently found in the vegetable kingdom. They generally contain the residues of aromatic bodies, and therefore will be discussed later. The simplest glucosides are the alkyl glucosides, which are produced in the action of HCl on alcoholic sugar solutions (Ber. **28**, 1151). Fehling's solution and phenylhydrazine at 100° do not affect the alkyl glucosides. However, they are decomposed into their components when boiled with dilute acids, or by ferments (p. 756).

α- and *β-Methylglucosides*, $C_6H_{11}O_6{\cdot}CH_3$, m.pp. 165° and 107°, are stereochemically different, the α-compound being dextrorotatory $[\alpha]_D = +157{\cdot}6°$, the β-body being lævorotatory $[\alpha]_D = -31{\cdot}85°$ (Ber. **34**, 2899) (configuration, see p. 690). They are formed together by the action of hydrochloric acid and methyl alcohol on dextrose, and can also be obtained from α- and β-acetochloro- or bromo-dextrose, methyl alcohol and silver carbonate, and hydrolysing the resulting tetraacetylmethylglucoside. β-Methylglucoside is formed from dextrose, dimethyl sulphate and alkali (Ber. **34**, 957, 2885: C. 1905, I. 1593). The α-compound is decomposed by invertin, but not the β-substance, which, however, is attacked by emulsin (Ber. **27**, R. 885: **27**, 2479, 2985: **28**, 1145). If α-methylglucoside be alkylated by means of silver oxide and iodomethane in methyl alcohol there is formed, among other compounds, *tetramethyl-α-methylglucoside*, b.p. 145°/17 mm.: the latter on hydrolysis yields 2 : 3 : 4 : 6-*tetramethylglucose*, m.p. 89°, b.p. 182–185°/26 mm.

γ-Methylglucoside (*methylglucofuranoside*) was obtained by Fischer (Ber. **47**, 1980) as a by-product in the preparation of α- and β-methylglucosides, and is a structural isomer of the latter containing a 1 : 4-oxide linkage. γ-Methylglucoside (which probably consists of a mixture of two stereoisomers) (J.C.S. **107**, 524) is differentiated from the ordinary glucosides by the following reactions:—(1) It is more rapidly oxidized by cold alkaline permanganate. (2) It is hydrolysed by the most dilute mineral acids. (3) It is very readily converted into a monoacetone compound. This reaction first observed with γ-methylglucoside seems to be a general property of furanose derivatives. α-Methylglucofuranoside has recently (J.C.S. **1932**, 2254) been obtained crystalline: unlike the impure substance, it does not instantaneously reduce permanganate.

β-Phenylglucoside, $C_6H_{11}O_5{\cdot}C_6H_5$, m.p. 175°, is obtained from β-acetochloroglucose and sodium phenate (Ber. **34**, 2898).

α- and *β-Pentaacetylglucose*, m.p. 112°, $[\alpha]_D + 101{\cdot}6°$, and m.p. 131°, $[\alpha]_D + 3°$. Preparation of partially acylated sugars, see Ber. **51**, 321.

α- and *β-Pentabenzoylglucose* (1 : 5 ring), m.p. 155–157°, $[\alpha]_D + 107{\cdot}6°$; m.p. 187°, $[\alpha]_D + 23{\cdot}7°$ (Ber. **51**, 321).

α- and *β-Pentabenzoyl-γ-glucose* (1 : 4 ring), m.p. 120°, $[\alpha]_D + 58{\cdot}6°$; m.p. 151°, $[\alpha]_D - 52{\cdot}6°$ (Ber. **60**, 1488).

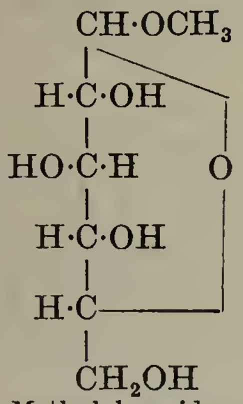
*α′-Acetochloroglucose,** $C_6H_7O(OAc)_4Cl$ (formerly β-acetochloroglucose), m.p. 74°, $[\alpha]_D + 165{\cdot}8°$ (CCl_4).

*β′-Acetochloroglucose,** m.p. 99°, $[\alpha]_D - 17{\cdot}4°$, is obtained from α′-acetobromoglucose by reaction with silver chloride (Ber. **61**, 287).

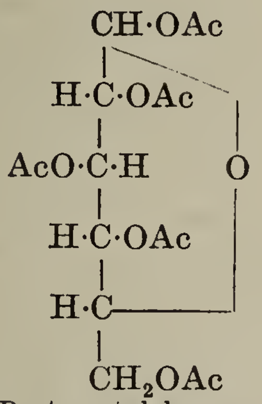
α′-Acetobromoglucose * (formerly β-acetobromoglucose), m.p. 89°, $[\alpha]_D + 199°$: *β′-acetobromoglucose* has not yet been obtained (Ber. **61**, 289).

The above compounds are closely related to the α- and β-alkylglucosides and have similar formulæ. α- and β-Pentaacetylglucose, which have entirely lost any aldehyde character, are formed from glucose and acetic anhydride in the presence of zinc chloride, sodium acetate or pyridine : the β- compound is converted into the α- by the action of zinc chloride or anhydrous stannic chloride (Ber. **61**, 137). If the pentaacetyl compounds are treated with liquid HCl or HBr, one acetyl group is replaced by halogen and the α′-acetobromo- or -chloroglucoses result (Ber. **34**, 2886). The α′-acetohalogenglucoses were first obtained by acting on glucose with acetyl chloride or bromide, the α′-chloro- compound being also obtained from β-pentaacetylglucose by the action of phosphorus pentachloride and aluminium chloride or anhydrous stannic chloride (Ber. **61**, 140). The β′-acetohalogenglucoses are very readily converted into the α′-compounds, and consequently can only be obtained under very special conditions (Ber. **61**, 140) or not at all (β′-acetobromoglucose). The acetohalogenglucoses are characterized by the ready reactivity of the halogen atom, which can be readily replaced by an acetyl or alkoxy group or by the nitrate group $O{\cdot}NO_2$: the product of the latter replacement is the well-crystallized *acetonitroglucose*, $C_6H_7O(OAc)_4{\cdot}ONO_2$, m.p. 151°, which can also be obtained from pentaacetylglucose and nitric acid (Ann. **331**, 381). By treating the acetohalogenglucose with methyl alcohol in the presence of silver carbonate, the methylglucosides are obtained (Ber. **34**, 957). The configuration of the halogen compound cannot, however, be deduced from that of the glucoside, as a Walden inversion usually takes place in this reaction.

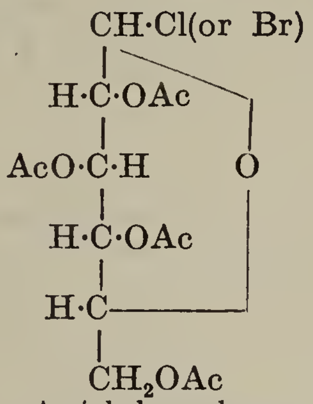
The compounds are represented by the following structural formulæ, the α- and β-compounds being stereoisomerides (p. 690) Ber. **34**, 957, 2885, 3205 : **35**, 853 : C. 1902, I. 180) :



Methylglucosides.



Pentaacetylglucoses.



Acetohalogenglucoses.

Glucosephosphoric Esters.—*Glucose*-3- or -4-*phosphoric acid*, $[\alpha]_D + 30{\cdot}7°$, is obtained from glucosediacetone and phosphoryl chloride in absolute pyridine (J. Biochem. (Japan) **6**, 31). *Glucosediphosphoric acid* : Biochem. Z. **32**, 173.

Hexosephosphoric esters are formed as intermediates in alcoholic fermentation. According to Harden and Young, who first directed attention to this, the formation of the zymophosphate (hexosediphosphoric acid) in the course of fermentation occurs according to the scheme (*cf.*, however, p. 141) :

$$2C_6H_{12}O_6 + 2K_2HPO_4 \longrightarrow 2CO_2 + 2C_2H_5OH + 2H_2O + C_6H_{10}O_4(PO_4K_2)_2.$$

The capacity of yeast to bring about this esterification seems to depend upon the presence of the enzyme complex : *cozymase* + *apozymase* (Biochem. Z. **161**, 244).

Phosphoric esters of substituted glucoses, see J. Biol. Chem. **48**, 233.

Nitrogenous glucosides have been obtained synthetically from acetobromo-

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* For nomenclature, see Ber. **59**, 1588.

glucose and purine and pyrimidine bases (Ber. **47**, 210, 1058, 1404, 1390): these compounds are closely related to the nucleic acids (*q.v.*).

Triaceto-1 : 6-*dibromoglucose*-<1 : 5> is obtained from lævoglucosan and phosphorus pentabromide (Helv. Chim. Acta. **5**, 187).

Methyl Ethers of Glucose.—These are obtained by the methylation of glucose by means of methyl iodide and silver oxide or of methyl sulphate and alkali. The methyl ethers of the methylglucosides are the products, and the methylglucoses obtained by splitting-off of the glucosidic hydroxyl. They are partially distillable in a high vacuum without decomposition.

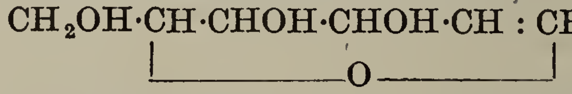
Tetramethyl-α-methylglucoside, a syrup, b.p. 108°/0·1 mm.: 2 : 3 : 4 : 6-*tetramethylglucose*-<1 : 5>, m.p. 88–89°, $[\alpha]_D$ + 83° (C. 1926, I. 881).

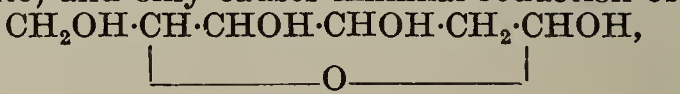
2 : 3 : 5 : 6-*Tetramethylglucose*-<1 : 4>, b.p. 122°/0·05 mm., is a derivative of γ-glucose (glucofuranose) and is obtained by methylation of γ-methylglucoside.

Mono-, *di*- and *trimethylglucoses* are usually obtained from the appropriate acetoneglucoses (see Ann. **440**, 1: Ber. **58**, 1547: J. Biol. Chem. **70**, 343).

6-*Triphenylmethylglucose*-<1 : 5>, $[\alpha]_D$ + 59·6° → + 38° (Ber. **58**, 872), is formed from glucose and triphenylchloromethane in absolute pyridine: it is of value for the introduction of groups into the 6-position in glucose.

Glucal, $CH_2OH\cdot\underbrace{CH\cdot CHOH\cdot CHOH\cdot CH}_{O} : CH$, is obtained from acetobromoglucose by reduction with zinc and acetic acid, *triacetylglucal* (m.p. 54–55°, $[\alpha]_D$ − 15·7°), being an intermediate product, which is hydrolysed by alcoholic ammonia to glucal (Ber. **54**, 450). Glucal has m.p. 60° (indefinite) and only causes minimal reduction of Fehling's solution. 2-*Desoxyglucose*, $CH_2OH\cdot\underbrace{CH\cdot CHOH\cdot CHOH\cdot CH_2\cdot CHOH}_{O}$, m.p. 148°, $[\alpha]_D$ + 46·6°, is obtained from glucal by the addition of water through the action of dilute sulphuric acid: it forms a phenylhydrazone, and glucosides, and is not fermented by yeast. *Hydroglucal*, m.p. 86–87°, $[\alpha]_D$ + 16·3°, is formed by the catalytic hydrogenation of glucal.





Anhydroglucoses.—(1) E. Fischer's *anhydroglucose*, m.p. 118°, $[\alpha]_D$ + 53·9° (Ber. **45**, 457, 3763).

(2) *Glucosan.*—1 : 2-*Anhydro-α-glucose*-<1 : 5> (Formula, see p. 693), m.p. 109°, $[\alpha]_D$ + 69·8°: formed by heating α-glucose in vacuo at 150–155° (Compt. rend. **171**, 243: Helv. Chim. Acta. **3**, 640), is smoothly fermented by yeast containing cozymase (Z. physiol. Chem. **170**, 23).

(3) *Lævoglucosan.*—1 : 6-*Anhydro-β-glucose*-<1 : 5> (Formula, see p. 693), m.p. 179·5°, $[\alpha]_D$ − 67·25°, from cellulose, starch or β-glucose by heating in vacuo at 200–300°, or from acetobromoglucose and trimethylamine (Helv. Chim. Acta. **4**, 819). Is not fermented by yeast.

Glucosyl chloride: from glucosan and concentrated hydrochloric acid.

d-*Glucose mercaptal*, $C_6H_{12}O_5(SC_2H_5)_2$, m.p. 127°, is obtained from d-glucose, mercaptan, and HCl. d-*Glucose ethylene mercaptal*, $C_6H_{12}O_5 : S_2C_2H_4$, m.p. 143°. d-*Glucose trimethylene mercaptal*, $C_6H_{12}O_5 : S_2C_3H_6$, m.p. 130°. d-*Glucosebenzyl mercaptal*, $C_6H_{12}O_5(SCH_2\cdot C_6H_5)_2$, m.p. 133° (Ber. **29**, 547).

Methylene glucose, $C_6H_{10}(CH_2)O_6$, m.p. 187° (Ber. **32**, 2585).

1 : 2-*Glucose monacetone*, $C_6H_{10}O_6 : C(CH_3)_2$, m.p. 156°. 1 : 2 : 5 : 6-*Diacetone glucose*-<1 : 4>, $C_6H_8O_6[C(CH_3)_2]_2$, m.p. 109°. $[\alpha]_D$ − 18·40: a derivative of γ-glucose (constitution, see Ber. **56**, 1243: J. Biol. Chem. **70**, 343).

d-*Chloralose*, m.p. 189°, and d-*Parachloralose*, $C_8H_{12}Cl_3O_6$, m.p. 227°, are two isomeric bodies, produced by the rearrangement of *d*-glucose with chloral (Ber. **27**, R. 471: **29**, R. 177).

***l*-Glucose**, m.p. 143°, is formed when the lactone of *l*-gluconic acid is reduced. It is perfectly similar to dextrose, but is lævorotatory, $[\alpha]_D$ (at equilibrium) = − 51·4°. Its *glucososazone* is, however, dextrorotatory. Its *diphenylhydrazone*, $C_6H_{12}O_5 : N\cdot N(C_6H_5)_2$, m.p. 163°, dissolves with difficulty (Ber. **23**, 2618).

***dl*-Glucose** results from the union of *d*- and *l*-glucose, and by the reduction of *dl*-gluconic lactone. *dl-Glucosazone*, m.p. 218°, is also formed from inactive mannose, and from synthetic α-acrose, or *dl*-fructose (p. 699) (Ber. **23**, 383, 2620).

(3) **Gulose**, $CH_2OH[CHOH]_4CHO$ (space formula, p. 705), the second

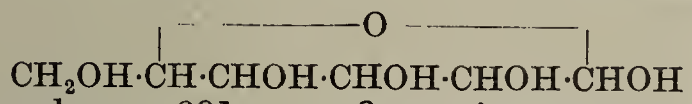
aldehyde of sorbitol, is likewise known in its three modifications. They are formed by the reduction of the lactones of the three gulonic acids (p. 713), and by further reduction yield the sorbitols. They are syrups and are not fermented by yeast. The name gulose is intended to indicate their relationship to glucose. l- and dl-*Gulose phenylhydrazone*, m.p. 143°. l-*Gulosazone*, m.p. 156°. dl-*Gulosazone*, m.p. 157–159°.

(4) *d*- and *l*-**Idoses** are prepared by the reduction of the idonic acids or their lactones (p. 714). They yield *d*- and *l*-iditol on reduction (p. 680) (space formula, p. 704).

(5) **Galactose** is the aldehyde of the alcohol dulcitol (which is inactive through internal compensation), and occurs in the three forms, *d*-, *l*- and *dl*-galactose.

The *dl*-**galactose,** m.p. 140–142°, results from the reduction of the lactone of *dl*-galactonic acid, and when fermented with beer yeast the *d*-form is fermented, leaving *l*-galactose ; *phenylhydrazone*, m.p. 158–160° ; *osazone*, m.p. 206°.

l-**Galactose,** m.p. 163° (p. 705), yields dulcitol on reduction, and mucic acid when it is oxidized ; *phenylhydrazone*, m.p. 158–160° ; *osazone*, m.p. 206°.

d-**Galactose,** 
$CH_2OH{\cdot}\overset{|\text{———O———}|}{CH{\cdot}CHOH{\cdot}CHOH{\cdot}CHOH{\cdot}CHOH}$ (1 : 5 ring, see Ber. **59,** 100 : see also p. 691 : configuration, see p. 705). It melts at 166°, is dextrorotatory and fermentable. *d*-Galactose is formed, together with glucose, by the hydrolysis of the disaccharide lactose, of the crystalline compound galactitol, $C_9H_{18}O_7$, which occurs in yellow lupins (Ber. **29,** 896) or of various gums, known as galactans (Ber. **20,** 1003). Galactose is important as a constituent of the cerebrosides. It is prepared by the hydrolysis of lactose by dilute sulphuric acid. Galactose yields dulcitol on reduction, and galactonic acid and mucic acid on oxidation. By the action of hydrogen cyanide and hydrochloric acid, it yields galactosecarboxylic acid. When warmed with alkali it is partly converted into *l*-sorbose, *d*-tagatose, *d*-talose and other compounds (*cf.* p. 687).

α- and *β-Methyl*-d-*galactosides*, m.p. 111° and 174°, $[\alpha]_D$ + 143·7° and + 30·7°, are obtained by the action of methyl alcoholic hydrochloric acid at 100° : the *β*-glycoside is hydrolysed by emulsin. By the action of methyl alcoholic hydrochloric acid a strongly lævorotatory methylgalactoside can also be obtained. This is probably a derivative of *γ*-galactose (1 : 4 ring) (J.C.S. **125,** 2468).

Tetramethyl-α- and *-β-methylgalactoside*, α-, b.p. 137°/11 mm., *β*-, m.p. 45° (C. 1904, II. 892).

2 : 3 : 5 : 6-*Tetramethylgalactose*-<1 : 4> is obtained by methylation of the above lævorotatory methylgalactoside. It does not crystallize and has $[\alpha]_D$ − 21·2° (no mutarotation). 2 : 3 : 4 : 6-*Tetramethylgalactose*-<1 : 5>, $[\alpha]_D$ + 109°, is obtained by direct methylation of galactose. 1 : 2 : 3 : 4-*Diacetonegalactose*-<1 : 5> is obtained from galactose and acetone and sulphuric acid, b.p. 131–139°/0·2 mm., $[\alpha]_{Hg\ yellow}$ − 60·9° (in tetrachloroethane) (Ber. **56,** 2122 : **59,** 100). *Triphenylmethylgalactose*, m.p. 73–75°.

Pentaacetylgalactose, m.p. 142°, *acetochlorogalactose*, m.p. 76° (82°), *acetobromogalactose*, m.p. 83°, and *acetonitrogalactose*, m.p. 94°. α- and *β-Galactose pentanitrate*, m.pp. 115° and 72° (Ber. **31,** 74). *Galactochloral*, m.p. 202° (Ber. **29,** 544).

Oxime, m.p. 175°, see p. 714. *Phenylhydrazone*, m.p. 158° ; *osazone*, m.p. 193°. *Galactose aminoguanidine chloride* (Ber. **28,** 2613). *Ethyl mercaptal*, m.p. 127° ; *ethylene mercaptal*, m.p. 149° (Ber. **29,** 547).

(6) *d*-**Talose,** $CH_2OH[CHOH]_4CHO$, is formed by the reduction of the lactone of *d*-talonic acid (p. 714) (Ber. **24,** 3625). Space formula, p. 706 ; *cf.* Ber. **27,** 383.

(7) **Rhamnohexose,** *methylhexose,* $CH_3\cdot CHOH(CHOH]_4\cdot CHO$, m.p. 181°, is produced by the reduction of rhamnose carboxylic acid; *osazone,* m.p. 200°. It forms methylheptonic acid with hydrocyanic and hydrochloric acids.

3 A. KETOHEXOSES

(1) **Fructose,** $CH_2\cdot CHOH\cdot CHOH\cdot CHOH\cdot C(OH)\cdot CH_2OH$, is known in the modifications *d*-, *l*- and *dl*-fructose.

d-**Fructose,** *lævulose, fruit sugar* (configuration, see p. 709: ring structure, *cf.* J.C.S. **1926,** 1858: Ber. **60,** 1168), m.p. 95°, occurs in almost all sweet fruits, together with dextrose. It was discovered in 1847 by Dubrunfaut. It is formed, (1) together with an equal amount of glucose, in the decomposition of sucrose, and is separated from the latter through the insolubility of its calcium compound (Ber. **28,** R. 46: C. 1928, I. 1280). As fructose rotates the plane of polarization more strongly towards the left than dextrose does to the right, the decomposition of the sucrose leads to the formation of a lævorotatory *invert sugar* solution (p. 725).

(2) On heating inulin with water to 100° for twenty-four hours, it is changed exclusively to lævulose (Ann. **205,** 162: Ber. **23,** 2107). It can also be obtained from secalose, a carbohydrate contained in green rye plants (Ber. **27,** 3525).

(3) It is formed together with *d*-mannose in the oxidation of *d*-mannitol; also (4) from *d*-glucosazone, which is obtained from *d*-glucose or *d*-mannose as well as *d*-fructose. This method of formation allies fructose genetically with *d*-dextrose and *d*-mannose (p. 693). Hence, in spite of its lævorotation of $[a]_D = -92{\cdot}3°$, it is called *d*-fructose.

Like glucose, fructose exists in two stereoisomeric forms, α- and β-*d*-fructose: the pure β-form has $[\alpha]_D - 133{\cdot}5°$, and in aqueous solution an equilibrium mixture is formed having $[\alpha]_D - 92{\cdot}3°$ (Ann. **257,** 166).

Fructose crystallizes with difficulty, and dissolves with greater difficulty than dextrose. By reduction it yields *d*-mannitol and *d*-sorbitol; and when oxidized the products are *d*-erythronic acid (p. 651) and glycollic acid. It is partially converted into *d*-dextrose and *d*-mannose by alkalis (p. 687). Heated under pressure with a little oxalic acid, *d*-fructose yields hydroxymethylfurfural (Ber. **28,** R. 786). It yields *d*-fructose carboxylic acid (p. 715) when treated with hydrocyanic and hydrochloric acids; this may be reduced to methylbutylacetic acid, whereby the constitution of fructose is proved. Phenylhydrazine and fructose yield *d*-glucosazone.

β-Methyl-d-*fructoside* (Ber. **28,** 1160), m.p. 119–120°, $[\alpha]_D - 173{\cdot}1°$ (J.A.C.S. **38,** 1216). 1 : 3 : 4 : 5-*Tetramethyl-β-methylfructoside,* m.p. 34°, $[\alpha]_D - 149°$ (in water). 1 : 3 : 4 : 5-*Tetramethylfructose*-<2 : 6>, m.p. 98–99°, $[\alpha]_D - 124$–121° (J.C.S. **121,** 2696: constitution, J.C.S. **1927,** 1040), is obtained by methylation of normal fructose. The isomeric 1 : 3 : 4 : 6-*tetramethylfructose*-<2 : 5>, b.p. 154°/13 mm., $[\alpha]_D + 30°$ (?), is obtained by hydrolysis of the methylation products of inulin and of cane sugar.

Phosphoric esters of fructose, see J. Biochem. (Japan), **6,** 31.

Diacetonefructose, α-compound, m.p. 118°, β-, m.p. 97°, are formed from fructose and acetone in presence of sulphuric acid (Ber. **57,** 1566). *Pentaacetylfructose*- <2 : 6>, α-form, m.p. 70°, $[\alpha]_D + 34{\cdot}7°$, β-form, m.p. 109°, $[\alpha]_D - 120{\cdot}5°$.

γ-Fructose, *fructofuranose* (2 : 5 oxide ring) (see J.C.S. **1927,** 1513), is unstable in the free condition and immediately reverts on isolation to normal fructopyranose. The sugar occurs linked to normal-glucose in cane sugar in the furanose form (Trehalose type, see p. 722) and in inulin, the fructose residues also exist in this form. In addition to the 1 : 3 : 4 : 6-tetramethylfructose described above, α- and *β-methylfructofuranosides* are known, $[\alpha]_D > +36{\cdot}5°$ and $-17°$ (Ber. **58**, 1842 : J.C.S. **121**, 2238).

Lævulosan (*fructosan*), m.p. 150°, $[\alpha]_D + 18{\cdot}6°$ (in water), is formed by heating fructose in vacuo at 120° (Helv. Chim. Acta. **4**, 613). *Heterolævulosan*, see Helv. Chim. Acta. **9**, 809.

Lævulochloral, m.p. 228° (Ber. **29**, R. 544). α- and *β-Lævulosan trinitrate*, $C_6H_7O_5(NO_2)_3$, m.p. 137° and 48° (Ber. **31**, 76).

l-**Fructose** is produced by fermenting *dl*- fructose (α-acrose) with yeast, whereby the *d*-modification is removed (Ber. **23**, 389).

dl-**Fructose** or **α-Acrose.**—The resolvable fructose modification is, by virtue of its own synthesis, of the greatest importance in the synthesis of sugars (p. 700).

Historical.—*Methylenitan*, the first compound resembling the sugars that was prepared, was obtained by Butlerow (1861), who condensed trioxymethylene (p. 236) with lime-water. O. Loew (1885) obtained *formose*, $(CH_2OH)_2C(OH){\cdot}CH(OH){\cdot}CO{\cdot}CH_2OH$ (?) (J. pr. Chem. **33**, 321 : C. 1897, I. 803, 906) in an analogous manner from trioxymethylene, and somewhat later the fermentable *methose*, by the use of magnesia (Ber. **22**, 470, 478). E. Fischer showed these three compounds to be mixtures of different hexoses, among which α-acrose occurs (Ber. **22**, 360). The latter, together with β-acrose, is obtained more easily by the action of barium hydroxide on acrolein bromide, $C_3H_4OBr_2$ (*E. Fischer* and *J. Tafel*, Ber. **20**, 1093), and also by the condensation of so-called *glycerose* or glyceric aldehyde, $CH_2OH{\cdot}CHOH{\cdot}CHO$, or dihydroxyacetone, $CH_2OH{\cdot}CO{\cdot}CH_2OH$ (Ber. **23**, 389, 2131 : **35**, 2630). Reduction converts *dl*-fructose or α-acrose into *dl*-mannitol or α-acritol.

(2) *d*-**Tagatose**, $C_6H_{12}O_6$, m.p. 124°, is formed by the action of potassium hydroxide solution on galactose. It is a ketose. *d*-Tagatose, galactose, and talose yield the same osazone, and therefore bear the same relation to one another as lævulose, dextrose, and mannitol. The above-mentioned alkali treatment also produces **galtose** and

(3) *l*-**Sorbose**, *ψ-Tagatose*, m.p. 154°, the optical isomer of

d-**Sorbose**, *sorbinose*, $C_6H_{12}O_6$, m.p. 154°. This is obtained from *d*-sorbitol (p. 680) by the action of *Bacterium xylinum*, and unites with *l*-sorbose to form *dl*-sorbose. *d*- and *l*-Sorbose yield on reduction, as well as *d*- and *l*-sorbitol, *d*- and *l*-iditol (p. 680). Sorbose stands to gulose and idose in the same relation as fructose to glucose and mannose (C. 1900, I. 758).

Hexose and Pentose Imines and Amines

Ammonia unites with the hexoses with loss of water to form dextrosimine, mannosimine, galactosimine, and forms with the pentoses arabinosimine, xylosimine, etc., which are decomposed by acids into the original aldoses and ammonia. Isomeric with the hexosimines is

d-**Glucosamine** *chitosamine*, $CH_2OH[CHOH]_3CH(NH_2)CHO$, m.p. 110° (decomp.) (Ber. **31**, 2476), obtained with other hexosamines, by hydrolysing with hydrochloric acid the *chitin* of the armour of lobsters, and from the cellulose of the fungus *Boletus edulis*; also from the hydrolysis of proteins, particularly mucin (see Ber. **34**, 3241, etc.). It is therefore of great physiological interest. It is prepared synthetically by reduction with sodium amalgam of the lactone of *d*-glucosaminic acid, which is formed from *d*-arabinosimine, hydrocyanic, and hydrochloric acids (Ber. **36**, 28). The compound was originally regarded by Fischer as a 2-aminoglucose, but more recent work by Levene has shown glucosamine to be really a 2-aminomannose (Biochem. Z. **124**, 27). It reacts with phenyl *iso*cyanate to form a *compound*, m.p. 211°, water being eliminated, and with phenylhydrazine yields glucosazone (p. 693). With hydroxylamine it yields *glucosamine oxime*, m.p. *c.* 122° (Ber. **31**, 2198). The action of nitrous acid does not produce glucose or mannose, but the unfermentable sugar *chitose*, $C_6H_{10}O_5$, is produced, which is regarded by Levene as a 2 : 5-anhydromannose (Ber. **36**, 2587). Oxidation with bromine water yields *d*-glucosaminic acid (p. 714) and oxidation by nitric acid, the dibasic chitonic or *iso*saccharic acid (p. 719).

Chondrosamine (2-*Aminotalose*, J. Biol. Chem. **31**, 609) is isomeric with glucosamine and is a constituent of the chondroglycoproteins (J. Biol. Chem. **26**, 143).

d-**Fructosamine** (iso*glucosamine*), $CH_2OH{\cdot}(CHOH)_3{\cdot}CO{\cdot}CH_2NH_2$, is obtained by the reduction of glucosazone, and on further reduction by sodium amalgam yields *d*-mannamine and *d*-glucamine (p. 681). With nitrous acid it forms *d*-fructose (Ber. **19**, 1920).

Other amino sugars have been synthesized. See Ber. **58**, 295 : **59**, 714.

The amino sugars, like the hexoses, form glucosides, which are obtained from the triacetylbromoaminohexoses and alcohols or phenols.

Thiosugars.—Thioglucosides are obtained from acetobromohexoses and the silver salt of alkyliminothiocarbonic esters :

$$\mathrm{R{\cdot}N : C(OEt){\cdot}S \,\vdots\, Ag + Br{\cdot} \,\vdots\, Hexose.}$$

These compounds on hydrolysis give the thiohexoses, which are obtained pure only with great difficulty (Ber. **47**, 1260, 2225 : **49**, 1638 : **50**, 793).

2 B. ALDOHEPTOSES, ALDOOCTOSES AND ALDONONOSES

(E. Fischer, Ann. **270**, 64.)

Just as aldohexoses can be built up from aldopentoses, so can aldoheptoses be obtained from aldohexoses, and aldooctoses from the aldoheptoses, etc.,—*e.g.* hydrocyanic acid is added to *d*-mannose, the lactone of *d*-mannoheptonic acid is then reduced to *d*-mannoheptose, which, subjected to the same reactions, yields *d*-mannooctose (see p. 687). The heptoses and octoses do not ferment, but mannononose is fermented by yeast. Heptitols, octitols and nonitols are formed in their reduction (p. 681).

d-**Mannoheptose**, $C_7H_{14}O_7$, m.p. 135° $[\alpha]_D^{20}$ + 68·6°, is obtained (1) from the lactone of mannoheptonic acid (p. 715) ; (2) perseitol yields it when oxidized (p. 681). Its *hydrazone*, m.p. about 198°, dissolves with difficulty ; *osazone*, m.p. about 200° (Ber. **23**, 2231). Sodium amalgam converts it into perseitol (p. 681). *l*-**Mannoheptose** (Ann. **272**, 186).

α-**Glucoheptose**, $C_7H_{14}O_7$, m.p. about 190° ; *osazone*, m.p. about 195° : best identified as 2 : 4-*dinitrophenylhydrazone*, m.p. 181°, or 2 : 4-*dinitrophenylosazone*, m.p. 232°. Preparation of pure sugar, Z. physiol. Chem. **167**, 37. Physiological behaviour, C. 1902, II. 634. β-**Glucoheptose**, Ann. **270**, 72, 87.

α-**Galaheptose**, $C_7H_{14}O_7$, from α-galaheptonic acid, forms an *osazone*, m.p. about 200° ; it is converted by hydrocyanic and hydrochloric acids into galaoctonic acid (p. 715). β-**Galaheptose**, m.p. (decomp.) 190–194°, is obtained from the lactone of β-galaheptonic acid (Ann. **288**, 139).

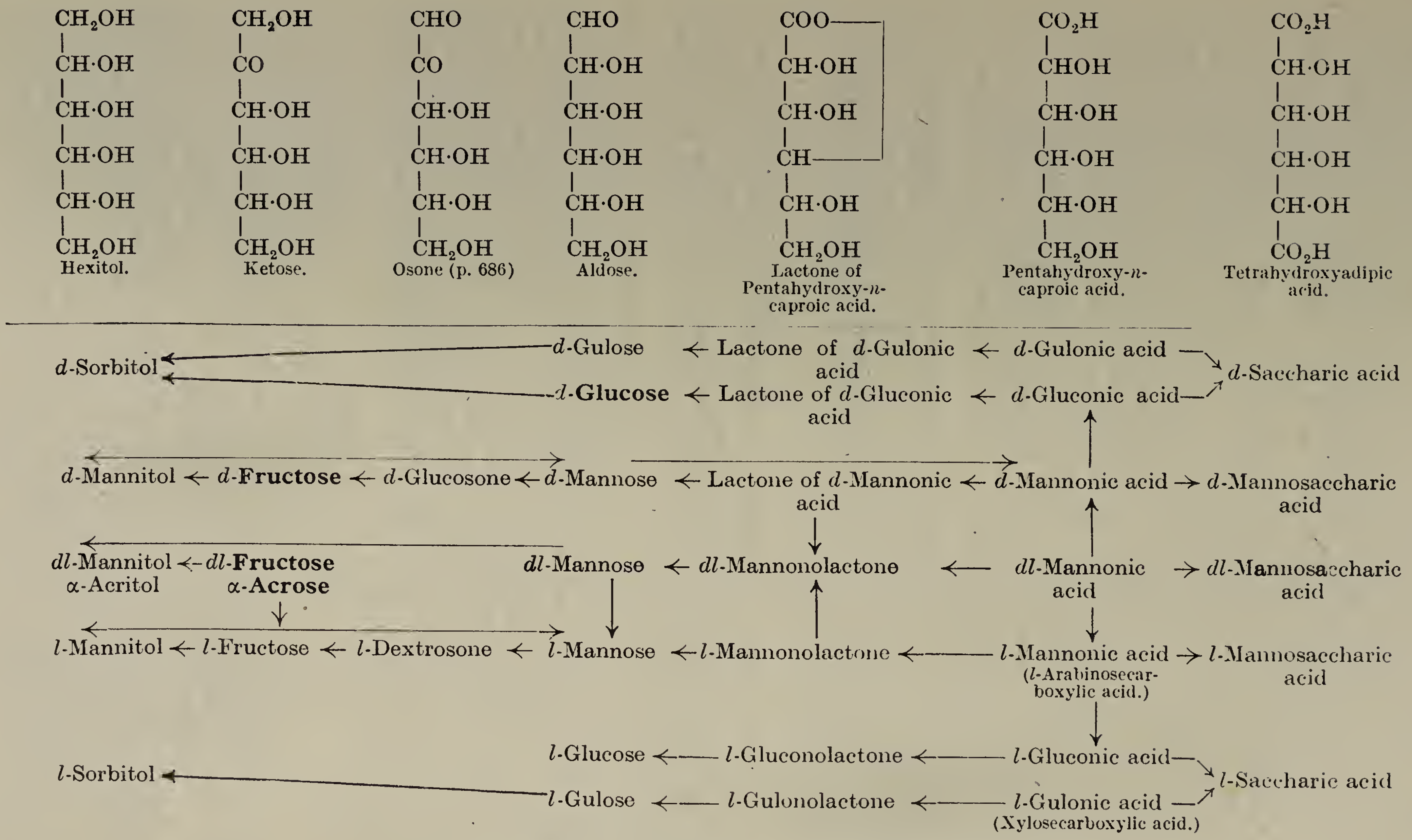
d-**Mannooctose**, $C_8H_{16}O_8$, is obtained from the lactone of mannooctonic acid (Ber. **23**, 2234). α-**Glucooctose** (Ann. **270**, 95). α-**Galaoctose** (Ann. **288**, 150).

d-**Mannononose**, $C_9H_{18}O_9$, obtained from the lactone of *d*-mannononoic acid, is very similar to dextrose, and ferments under the influence of yeast ; *hydrazone*, m.p. 223° ; *osazone*, m.p. about 227° (Ber. **23**, 2237). **Glucononose** (Ann. **270**, 104).

Synthesis of *d*-Glucose and *d*-Fructose

As already mentioned, Emil Fischer succeeded in isolating α-acrose or *dl*-fructose from the condensation products of glycerose (p. 589) and formaldehyde (p. 235). He used this as the parent substance for the synthesis, not only of *d*-glucose and *d*-fructose, but also of *d*-mannose, *d*-mannitol, *d*-sorbitol and the *l*-enantiomorphs of these substances. The relationships between the compounds is shown on p. 701.

The reduction product of α-acrose, α-acritol or *dl*-mannitol is difficult to obtain in reasonable quantity by the synthesis of α-acrose by aldol condensation of glycerose and subsequent reduction, and for this reason, its constitution having been established, Fischer obtained further quantities by the following process. *d*-Mannitol is oxidized to *d*-mannose and the latter to *d*-mannonic acid, which readily yields a lactone by loss of water. *l*-Arabinose combines with hydrogen cyanide to form the nitrile of *l*-arabinosecarboxylic acid, or *l*-mannonic acid. From the latter a lactone is also obtained, and by mixing equal amounts of the



NOTE.—Hexoses are for simplicity written in the open aldehyde form.

d- and *l*-isomers, *dl*-mannonolactone is obtained, which, on reduction, yields successively *dl*-mannose and *dl*-mannitol, the latter being identical with α-acritol.

dl-Mannonic acid, like racemic acid (p. 656), can be resolved by strychnine and morphine into *d*- and *l*-mannonic acid. By the reduction, on the one hand, of the lactone of *d*-mannonic acid, d-*mannose* and d-*mannitol* are formed, and, on the other hand, *d*-mannose and phenylhydrazine yield *d*-glucosazone, which can also be obtained from *d*-glucose, and lævulose or *d*-fructose.

d-Glucosazone yields dextrosone (p. 686), and the latter by reduction forms *lævulose* or d-*fructose.*

To pass from *d*-mannonic acid to *d*-glucose, the former is heated to 140° with quinoline, whereby it is then partially converted into *d*-gluconic acid. Conversely, the latter under the same conditions changes in part to *d*-mannonic acid (*cf.* the intertransformation of *d*-dextrose and *d*-mannose, by the action of alkalis, (p. 687). *d-Glucose* or grape sugar is formed in the reduction of the lactone of *d*-gluconic acid. d-*Sorbitol* is produced when grape sugar is reduced. Proceeding from *l*-mannonic acid, the corresponding *l*-derivatives are similarly obtained. l-*Fructose* is left by the fermentation of *dl*-fructose or α-acrose, and l-*mannose* in like manner from *dl*-mannose.

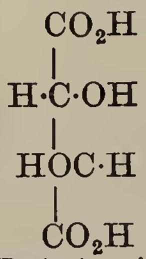
The gulose group and the sugar-acids, produced in the oxidation of the pentahydroxy-*n*-caproic acids, are also considered in the table. d-*Saccharic acid*, resulting from the oxidation of *d*-gluconic acid, yields *d*-gulonic acid on reduction, and the lactone of the latter by similar treatment changes to d-*gulose*, the second aldehyde of *d*-sorbitol.

The aldohexoses are connected with the aldopentoses (1) through l-*arabinose*, which, by the addition of HCN, as already mentioned, yields arabinosecarboxylic acid or *l*-mannonic acid, and *l*-gluconic acid ; (2) through the *xyloses*, the HCN-addition product of which is the nitrile of xylosecarboxylic acid, or *l*-gulonic acid. Oxidation changes *l*-gulonic acid to *l*-saccharic acid. l-*Gulose* and l-*sorbitol* are formed in the reduction of its lactone.

A. The Space-Isomerism of the Pentitols and Pentoses

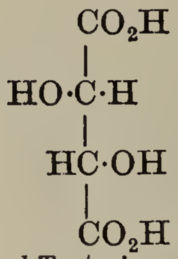
J. H. van 't Hoff, Die Lagerung der Atome in Raum (Trans. Herrmann, Vieweg, Braunschweig, 1908 : *Hantzsch*, Grundriss der Stereochemie, Leipzig, 1904 : *Werner*, Lehrbuch der Stereochemie, Fischer, Jena, 1904 : *Wedekind*, Stereochemie, Berlin, 1923.)

The structural formula of the normal, simplest pentitol : $CH_2OH{\cdot}\overset{*}{C}HOH{\cdot}CHOH{\cdot}\overset{*}{C}HOH{\cdot}CH_2OH$, contains two asymmetric carbon atoms. The CHOH-group standing between them is the cause of two possible inactive modifications instead of one (the case with the tartaric acids), as the result of an internal compensation. Furthermore, theory permits of two optically active modifications, and a fifth optically inactive form, arising from the union of the two optically active varieties. This is the racemic or *dl*-modification, corresponding with *dl*-tartaric acid or racemic acid. These relations are most quickly and readily made clear by means of the atomic models. The molecule-model is projected upon the surface of the paper, and then formulæ similar to those observed with tartaric acid are derived :



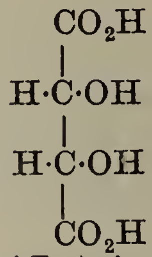
$$\begin{array}{c} CO_2H \\ | \\ H{\cdot}C{\cdot}OH \\ | \\ HOC{\cdot}H \\ | \\ CO_2H \end{array}$$

d-Tartaric acid.



$$\begin{array}{c} CO_2H \\ | \\ HO{\cdot}C{\cdot}H \\ | \\ HC{\cdot}OH \\ | \\ CO_2H \end{array}$$

l-Tartaric acid.



$$\begin{array}{c} CO_2H \\ | \\ H{\cdot}C{\cdot}OH \\ | \\ H{\cdot}C{\cdot}OH \\ | \\ CO_2H \end{array}$$

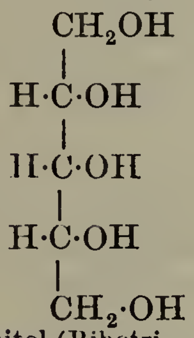
i-Tartaric acid.

The formulæ for the four stereochemically different pentitols arise in the same manner as in the case of the tartaric acids. Suppose these four pentitols to be oxidized, in one instance the upper CH_2OH-group, and then the lower similar group having been converted into the CHO-group, there will result eight stereochemically different aldopentose formulæ, none of which passes into any other by a rotation of 180°. The number of predicted space-isomers with *n* symmetric carbon atoms and with an asymmetric formula may be more easily deduced by applying the 2^n formula of van 't Hoff, in which n indicates the number of asymmetric carbon atoms. In the aldopentoses $n = 3$, hence $2^n = 2^3 = 8^3$:

Pentitol (and Trihydroxyglutaric acids).

Aldopentoses (and Pentone acids).

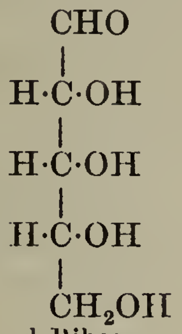
(1)



$$\begin{array}{c}\mathrm{CH_2OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CH_2\cdot OH}\end{array}$$

Adonitol (Ribotrihydroxyglutaric acid).

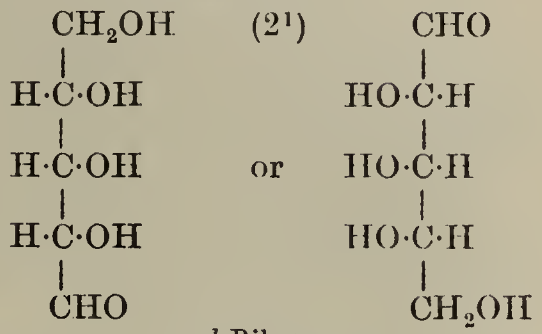
(1¹)



$$\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CH_2OH}\end{array}$$

d-Ribose.

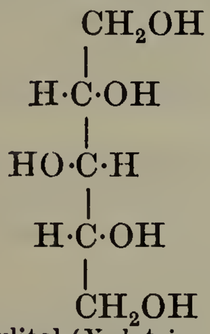
(2¹)



$$\begin{array}{c}\mathrm{CH_2OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CHO}\end{array}\quad \text{or} \quad \begin{array}{c}\mathrm{CHO}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{CH_2OH}\end{array}$$

l-Ribose (*l*-Ribonic acid).

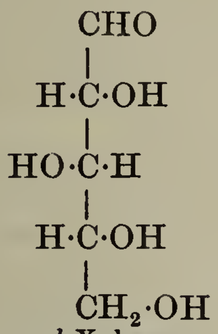
(2)



$$\begin{array}{c}\mathrm{CH_2OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CH_2OH}\end{array}$$

Xylitol (Xylotrihydroxyglutaric acid).

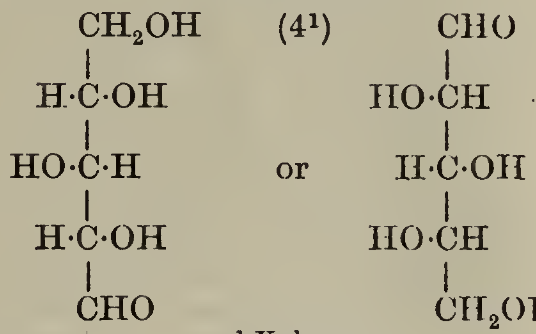
(3¹)



$$\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CH_2\cdot OH}\end{array}$$

l-Xylose (*l*-Xylonic acid).

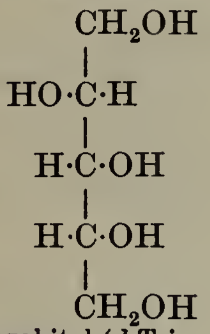
(4¹)



$$\begin{array}{c}\mathrm{CH_2OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CHO}\end{array}\quad \text{or} \quad \begin{array}{c}\mathrm{CHO}\\|\\\mathrm{HO\cdot CH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{HO\cdot CH}\\|\\\mathrm{CH_2OH}\end{array}$$

d-Xylose.

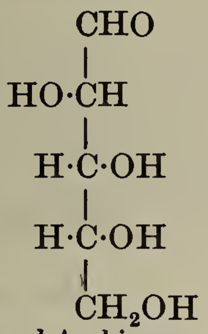
(3)



$$\begin{array}{c}\mathrm{CH_2OH}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CH_2OH}\end{array}$$

d-Arabitol (*d*-Trihydroxyglutaric acid).

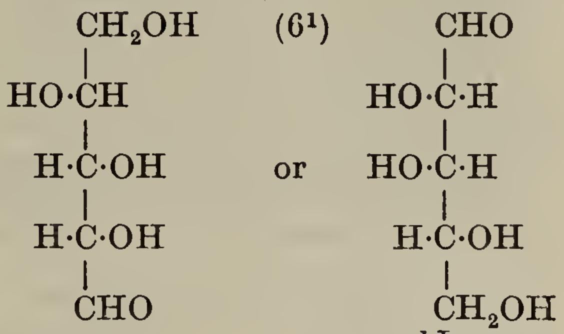
(5¹)



$$\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{HO\cdot CH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CH_2OH}\end{array}$$

d-Arabinose (*d*-Arabonic acid).

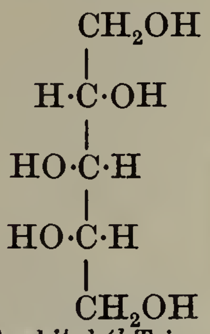
(6¹)



$$\begin{array}{c}\mathrm{CH_2OH}\\|\\\mathrm{HO\cdot CH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CHO}\end{array}\quad \text{or} \quad \begin{array}{c}\mathrm{CHO}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{CH_2OH}\end{array}$$

d-Lyxose (*d*-Lyxonic acid).

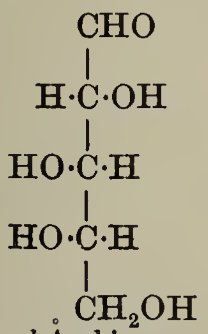
(4)



$$\begin{array}{c}\mathrm{CH_2OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{CH_2OH}\end{array}$$

l-Arabitol (*l*-Trihydroxyglutaric acid).

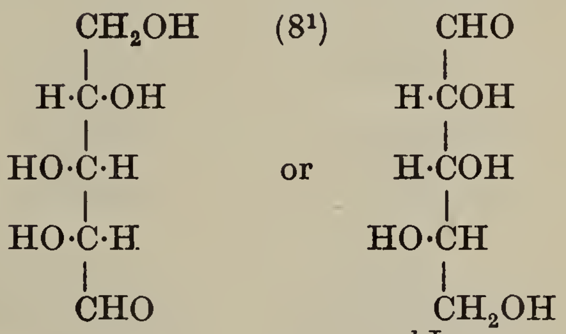
(7¹)



$$\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{CH_2OH}\end{array}$$

l-Arabinose (*l*-Arabonic acid.)

(8¹)



$$\begin{array}{c}\mathrm{CH_2OH}\\|\\\mathrm{H\cdot C\cdot OH}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{HO\cdot C\cdot H}\\|\\\mathrm{CHO}\end{array}\quad \text{or} \quad \begin{array}{c}\mathrm{CHO}\\|\\\mathrm{H\cdot COH}\\|\\\mathrm{H\cdot COH}\\|\\\mathrm{HO\cdot CH}\\|\\\mathrm{CH_2OH}\end{array}$$

l-Lyxose.

The stereoisomeric aldopentoses are capable naturally of uniting to four inactive double molecules, which can be resolved. The space-formulæ (7¹) and (3¹) for ordinary or *l*-arabinose and the xyloses follow from the intimate connection of the *l*-arabinoses with *l*-glucose, and the xyloses with *l*-gulose, as will be shown later (p. 709).

If the space-formula of inactive xylitol may be considered as established, there remains but one possible formula for inactive adonitol, the reduction product of ribose.

Four trihydroxyglutaric acids (p. 677) correspond with the four theoretically predicted pentitols. The same number of eight space isomers as indicated by the pentoses are possible also for the corresponding monocarboxylic acids, the tetrahydroxy-*n*-valeric acids, as well as for their corresponding aldehydocarboxylic acids, and also for the ketoses of the hexitol series, to which fructose belongs.

B. The Space-Isomerism of the Hexitols, the Aldohexoses and the Gluconic Acids

The structural formula of the normal and simplest hexitol:

$CH_2OH\cdot\overset{*4}{C}HOH\cdot\overset{*3}{C}HOH\cdot\overset{*2}{C}HOH\cdot\overset{*1}{C}HOH\cdot CH_2OH$, contains four asymmetric carbon atoms. The theory of van 't Hoff and Le Bel permits of ten possible space-isomeric configurations for such a compound.

In tartaric acid (p. 653) we started with the point of union of the two asymmetric carbon atoms in determining the successive series; and in hexitol also we begin in the middle of the molecule, and then compare C-atom 1 with C-atom 4, and C-atom 2 with C-atom 3. In this manner the ten hexitol configurations given below have been derived.

If in each of the ten hexitols, in one instance the upper —CH_2OH group, and in another the lower —CH_2OH group 2, have been oxidized to aldoses, then twenty space-isomeric aldohexoses would result. However, each of the four hexitols (Nos. 1, 2, 3, and 4) yields two aldoses, whose formulæ by a rotation of 180° pass into each other, which consequently would reduce the number of possible space-isomeric aldohexoses to 16.

Ten tetrahydroxyadipic acids (*saccharic acids*) correspond with the ten space-isomeric hexitols; sixteen pentahydroxy-*n*.-valeric or hexonic acids (*gluconic acids*), and sixteen aldehydotetrahydroxymonocarboxylic acids (*glucuronic acids*) correspond with the sixteen space-isomeric aldohexoses.

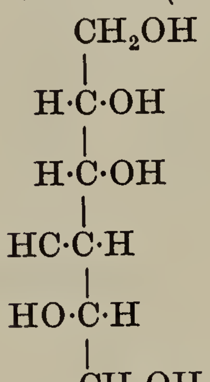
The hexitols and the tetrahydroxyadipic acids also have four inactive, racemic or *dl*-modifications, the aldohexoses, hexonic acids, and aldehydotetrahydroxycarboxylic acids, also 8 *dl*-modifications, as is evident from an inspection of the formulæ in the appended table.

The number of theoretically possible space-isomeric aldohexoses, containing four asymmetric carbon atoms in the molecule, are more readily derived by employing the van 't Hoff formula 2^n given above with the aldopentoses. This for 2^4 would give sixteen space-isomeric aldohexoses.

The space-isomerism of the ketohexoses, containing three asymmetric C-atoms, has been included in the isomerism of the aldopentoses (p. 703).

Hexitols (and Saccharic acids).

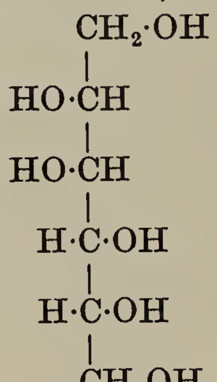
(1)



$$\begin{array}{c} CH_2OH \\ | \\ H\cdot C\cdot OH \\ | \\ H\cdot C\cdot OH \\ | \\ HC\cdot C\cdot H \\ | \\ HO\cdot C\cdot H \\ | \\ CH_2OH \end{array}$$

l-Mannitol
(*l*-Mannosaccharic acid).

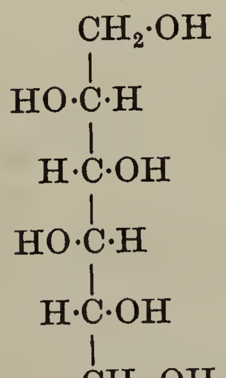
(2)



$$\begin{array}{c} CH_2\cdot OH \\ | \\ HO\cdot CH \\ | \\ HO\cdot CH \\ | \\ H\cdot C\cdot OH \\ | \\ H\cdot C\cdot OH \\ | \\ CH_2OH \end{array}$$

d-Mannitol
(*d*-Mannosaccharic acid).

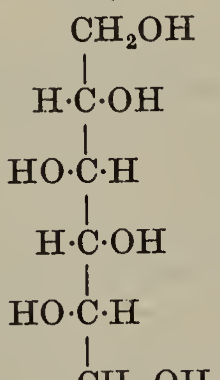
(3)



$$\begin{array}{c} CH_2\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ H\cdot C\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ H\cdot C\cdot OH \\ | \\ CH_2\cdot OH \end{array}$$

l-Iditol
(*l*-Idosaccharic acid).

(4)

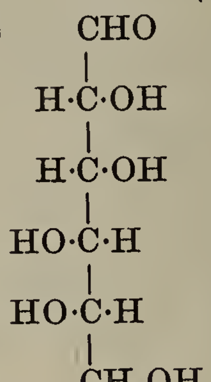


$$\begin{array}{c} CH_2OH \\ | \\ H\cdot C\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ H\cdot C\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ CH_2\cdot OH \end{array}$$

d-Iditol
(*d*-Idosaccharic acid).

Aldohexoses (and Hexonic acids).

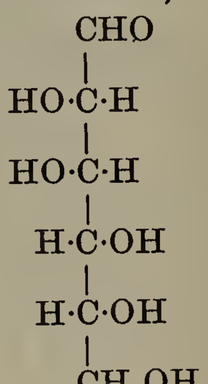
(1¹)



$$\begin{array}{c} CHO \\ | \\ H\cdot C\cdot OH \\ | \\ H\cdot C\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ HO\cdot C\cdot H \\ | \\ CH_2OH \end{array}$$

l-Mannose
(*l*-Mannonic acid).

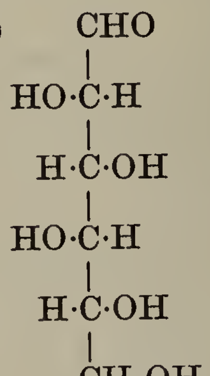
(2¹)



$$\begin{array}{c} CHO \\ | \\ HO\cdot C\cdot H \\ | \\ HO\cdot C\cdot H \\ | \\ H\cdot C\cdot OH \\ | \\ H\cdot C\cdot OH \\ | \\ CH_2OH \end{array}$$

d-Mannose
(*d*-Mannonic acid).

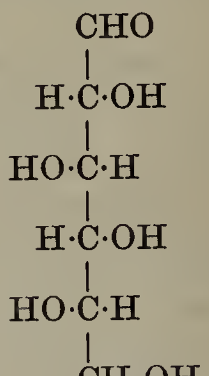
(3¹)



$$\begin{array}{c} CHO \\ | \\ HO\cdot C\cdot H \\ | \\ H\cdot C\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ H\cdot C\cdot OH \\ | \\ CH_2OH \end{array}$$

l-Idose
(*l*-Idonic acid).

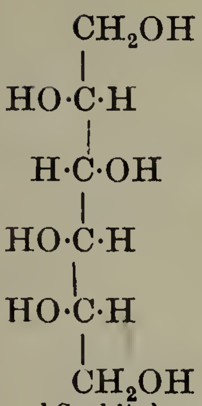
(4¹)



$$\begin{array}{c} CHO \\ | \\ H\cdot C\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ H\cdot C\cdot OH \\ | \\ HO\cdot C\cdot H \\ | \\ CH_2OH \end{array}$$

d-Idose
(*d*-Idonic acid).

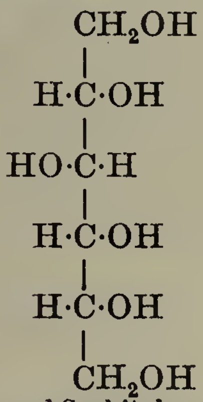
(5)



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

l-Sorbitol
(*l*-Saccharic acid).

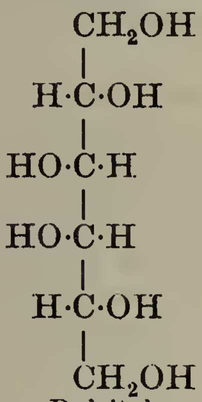
(6)



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

d-Sorbitol
(*d*-Saccharic acid).

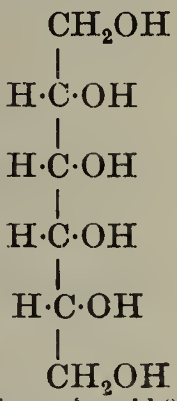
(7)



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

Dulcitol
(Mucic acid).

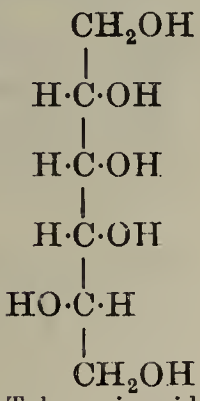
(8)



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

(Allomucic acid ?).

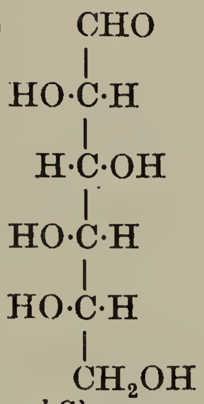
(9)



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

(*l*-Talomucic acid).

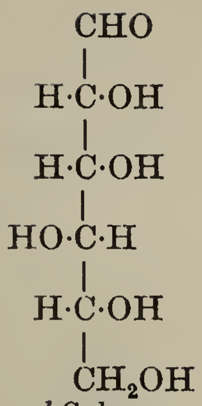
(5^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

l-Glucose
(*l*-Gluconic acid).

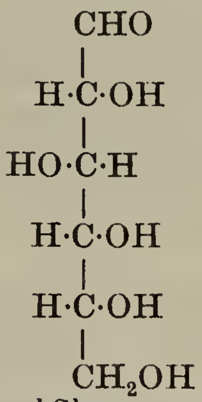
(6^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

l-Gulose
(*l*-Gulonic acid).

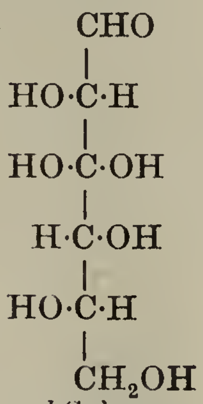
(7^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

d-Glucose
(*d*-Gluconic acid).

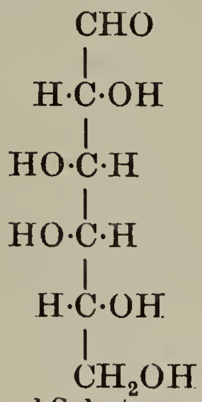
(8^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

d-Gulose
(*d*-Gulonic acid).

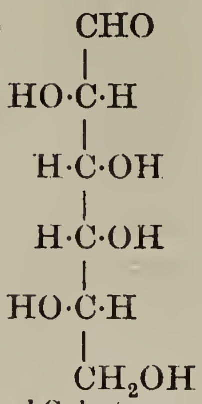
(9^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

d-Galactose
(*d*-Galactonic acid).

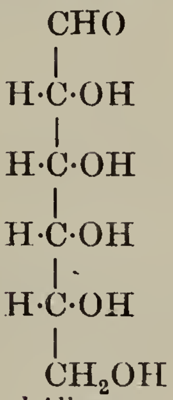
(10^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

l-Galactose
(*l*-Galactonic acid).

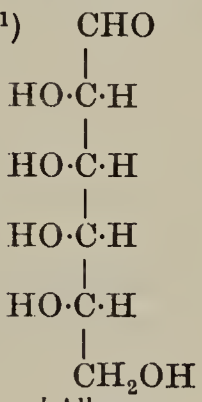
(11^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

d-Allose.

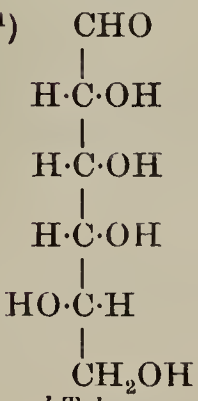
(12^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

l-Allose.

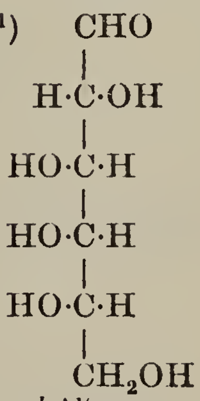
(13^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

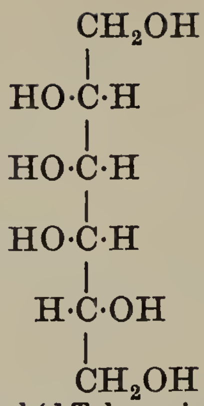
l-Talose.

(14^1)

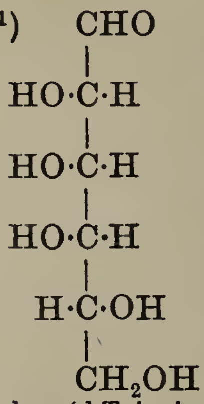


$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

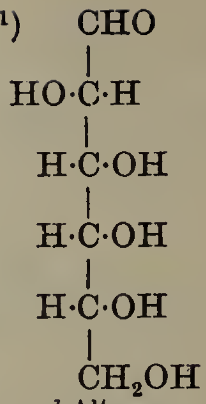
l-Altrose.

(10)


d-Talitol (*d*-Talomucic acid).

(15^1)


d-Talose (*d*-Talonic acid).

(16^1)


d-Altrose.

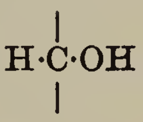
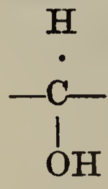
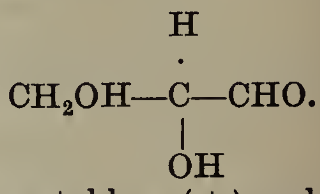
To render rational names possible, E. Fischer has proposed to indicate the configuration by the sign + or —. These are not intended to show the influence of the individual asymmetric carbon atom upon the optical properties of the molecule, as van 't Hoff formerly expressed it, but merely the position of a substituent upon the right or left side of the preceding configuration formulæ. (See also Ber. **40**, 102.) The formula should be so viewed that in the sugars the aldehyde or ketone group, and in the monobasic acids the carboxyls, stand above. The numbers begin above, and the sign + or — represents the position of hydroxyl, *e.g.*:

Grape sugar, *d*-dextrose = Hexanepentolal + — + + (Formula 7^1).
d-Gluconic acid . . = Hexanepentol acid + — + + (Formula 7^1).
Lævulose, *d*-fructose . = Hexanepentol-2-one — + +.

"In the case of symmetrical structure,—as it exists, for example, in the diacids and alcohols of the sugar group,—there is no favoured position; consequently, presuming that the numbering invariably proceeds from the top down, we get a doubled steric designation," *e.g.*:

d-Saccharic acid . = Hexanetetrol diacid + — + + or — — + —
Dulcitol . . = Hexanehexol . + — — + or — + + —

A similar derivation of the projected space-formulæ of the hexoses is carried out by Wohl and Freudenberg (Ber. **56**, 309), starting from *d*-glyceraldehyde (dextrorotatory), which is connected with *d*-glucose by way of tartaric acid.

For this system it is necessary only to have a convention that the carbonyl group of the hexose (in agreement with E. Fischer) is written to the right in a horizontal formula, or at the top in a vertically written formula, and the configuration

$\overset{|}{\underset{|}{H\cdot C\cdot OH}}$
or

$\overset{H}{\underset{OH}{-C-}}$
of the adjacent carbon atom is described as *d*-, *d*-glyceraldehyde having on this basis the projected formula

$CH_2OH-\overset{H}{\underset{OH}{C}}-CHO$.

The configuration of various sugars is deduced in the following table. (+) and (—) denote the actual direction of rotation.

Triose.	Tetroses.	Pentoses.	Hexoses.
d = *d*(+) Glyceraldehyde	dd = *d*(—) Erythrose	ddd = *d*(—)ribose	dddd = *d*-Allose dddl = *d*-Altrose
		ddl = *d*(—)Arabinose	ddld = *d*-Glucose ddll = *d*-Mannose
	dl = *d*-Threose	dld = *d*(+) Xylose	dldd = *d*(+)Gulose dldl = *d*(+)Idose
		dll = *d*(—)Lyxose	dlld = *d*(+)Galactose dlll = *d*(+)Talose

Derivation of the Space-formula for d-Glucose or Grape Sugar

The following relations arranged first in the diagram are the basis of this derivation :

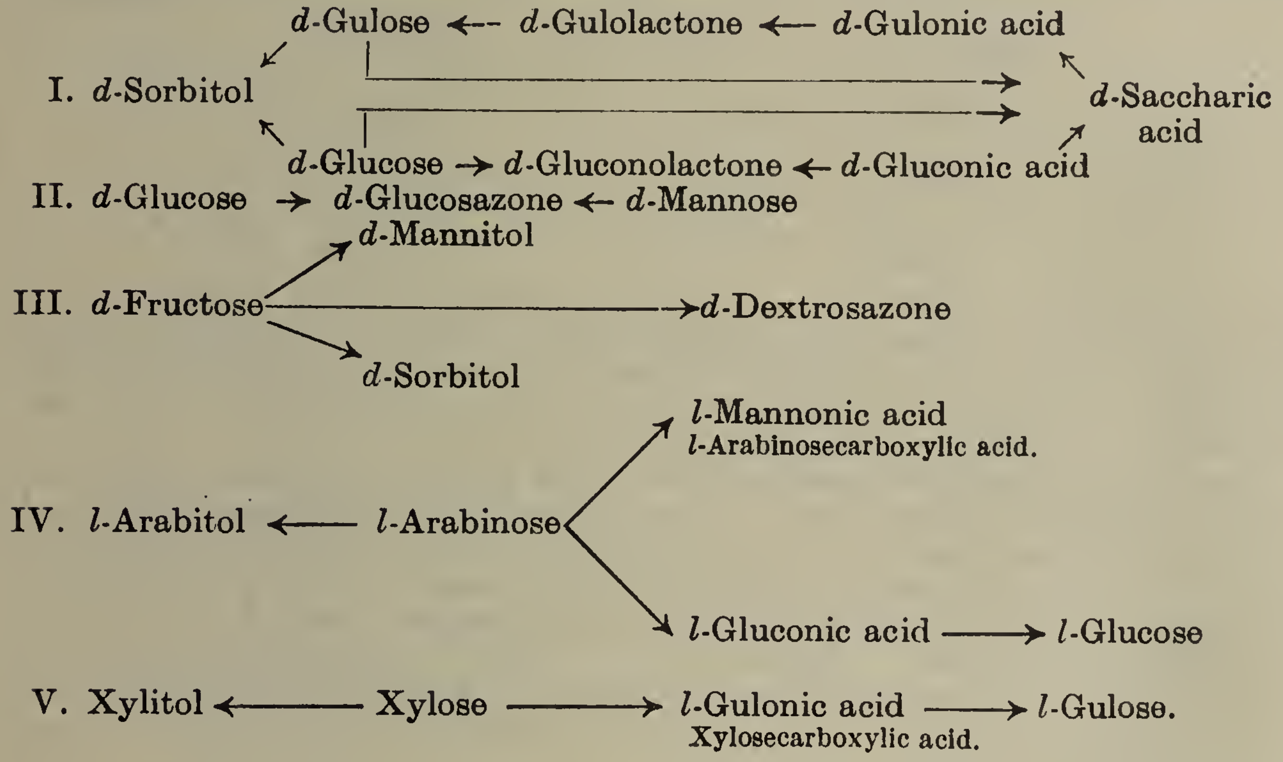
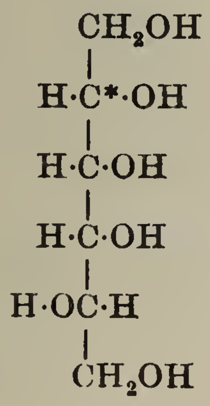


Diagram I shows that *d*-glucose or grape sugar and *d*-gulose yield the same *d*-saccharic acid. Hence it follows that *d*-saccharic acid and the *d*-sorbitol corresponding with it cannot have the formulæ (1), (2), (3), (4) (p. 704), because it is only the hexitols and saccharic acids, (5), (6), (7), (8), (9), (10), which yield two space-isomeric aldohexoses each. The formulæ (7) and (8) of the six space-formulæ represent, by virtue of internal compensation, optically inactive molecules, which therefore disappear for the optically active *d*-saccharic acid and *d*-sorbitol.

The fact that *d*-saccharic acid and *d*-mannosaccharic acid, *d*-gluconic and *d*-mannonic acids, *d*-dextrose and *d*-mannose, *d*-sorbitol and *d*-mannitol, only differ by the varying arrangement of the univalent atoms or atomic groups with reference to the carbon atom, which in *d*-dextrose and *d*-mannose is linked to the aldehydo-group, makes it possible to decide between the stereoisomeric formulæ (5) and (6), (9) and (10) ; for *d*- and *l*-saccharic acid, *d*-mannose and *d*-glucose, yield the same osazone (diagram II, above). *l*-Arabinose treated with hydrocyanic and hydrochloric acids gives rise to both *l*-mannonic or *l*-arabinosecarboxylic acid, and *l*-gluconic acid (diagram IV, above). The same relations which are observed with *l*-mannonic and *l*-gluconic acid prevail naturally with their stereoisomers—*d*-mannonic acid and *d*-gluconic acid. A mixture of *d*-mannitol and *d*-sorbitol is obtained by the reduction of *d*-fructose.

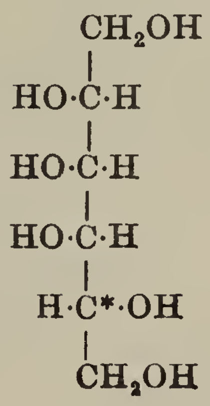
Assuming that *d*-sorbitol and *d*-saccharic acid possessed the space-formulæ (9) or (10) (p. 705) :

(9)



$$\begin{array}{c} CH_2OH \\ | \\ H\cdot C^*\cdot OH \\ | \\ H\cdot C\cdot OH \\ | \\ H\cdot C\cdot OH \\ | \\ H\cdot OC\cdot H \\ | \\ CH_2OH \end{array}$$

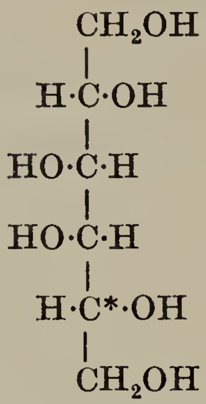
(10)



$$\begin{array}{c} CH_2OH \\ | \\ HO\cdot C\cdot H \\ | \\ HO\cdot C\cdot H \\ | \\ HO\cdot C\cdot H \\ | \\ H\cdot C^*\cdot OH \\ | \\ CH_2OH \end{array}$$

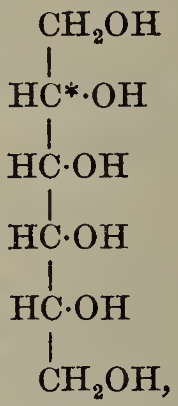
then *d*-mannitol, and also *d*-mannosaccharic acid, would have the formulæ (7) or (8):

(7)



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C^{*}\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

(8)



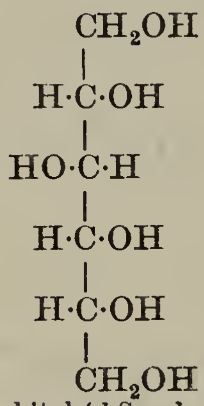
$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{HC^{*}\cdot OH} \\ | \\ \mathrm{HC\cdot OH} \\ | \\ \mathrm{HC\cdot OH} \\ | \\ \mathrm{HC\cdot OH} \\ | \\ \mathrm{CH_2OH,} \end{array}$$

because only these formulæ differ from (9) and (10) exclusively in the varying arrangement of the atoms or atom groups with reference to the asymmetric carbon atoms designated by asterisks. However, formulæ (7) and (8) by internal compensation give rise to inactive molecules, consequently cannot give the configuration of *d*-mannitol and *d*-mannosaccharic acid.

Thus, for *d*-sorbitol and *l*-sorbitol, *d*-saccharic acid and *l*-saccharic acid there remain only formulæ (5) and (6), from which (6) is arbitrarily selected for *d*-sorbitol and *d*-saccharic acid, and (5) for *l*-sorbitol and *l*-saccharic acid. "When this has been done then all further arbitrary selection ceases; now the formulæ for all optically active compounds connected experimentally with saccharic acid are regarded as established" (Ber. **27**, 3217). Hence, the space-formula (2) falls to *d*-mannitol and *d*-mannosaccharic acid, and formula (1) to *l*-mannitol and *l*-mannosaccharic acid, which would also give formulæ (2) and (1^1) to *d*- and *l*-mannonic acids (p. 704).

The aldohexoses (7^1) and (8^1) (p. 705) correspond with *d*-sorbitol and the saccharic acid with space-formula (6):

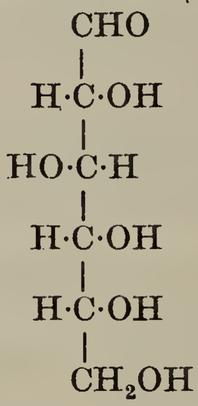
(6)



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

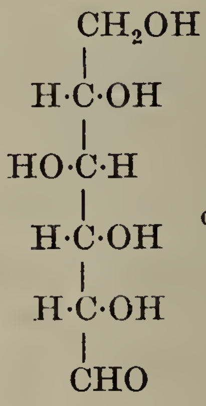
d-Sorbitol (*d*-Saccharic acid).

(7^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

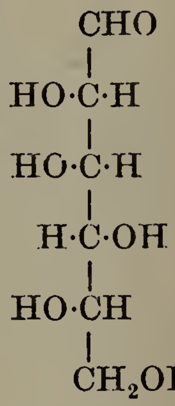
$\underline{(8^1)}$



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CHO} \end{array}$$

or when rotated 180°

(8^1)



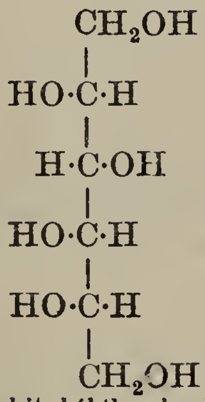
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot CH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

In order to obtain the aldehyde group at the top of the formula image, formula $\underline{(8^1)}$ must be turned 180°. This converts it into formula (8^1), and the succession of the atomic groups attached to the asymmetric carbon atom is naturally not altered.

The choice between formulæ (7^1) and (8^1) for *d*-dextrose and *d*-gulose still remains. We are able to determine this if we can select out the space-formulæ for the two stereoisomers—*l*-glucose and *l*-gulose. This is possible with a proper consideration of the genetic relation of the last two bodies with *l*-arabinose and xylose, as represented in diagrams IV and V (p. 707).

The formulæ (5^1) and $\underline{(6^1)}$ of the aldohexoses correspond with the formula (5) of *l*-saccharic acid. $\underline{(6^1)}$ when rotated becomes (6^1):

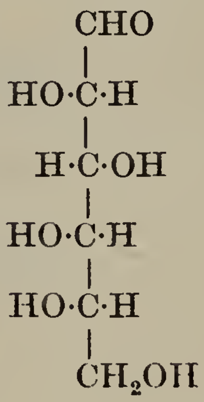
(5)



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

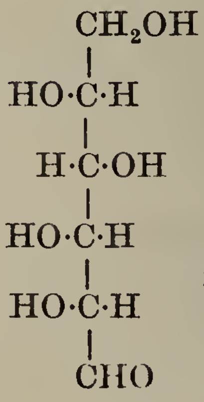
l-Sorbitol (*l*.Saccharic acid).

(5^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CH_2OH} \end{array}$$

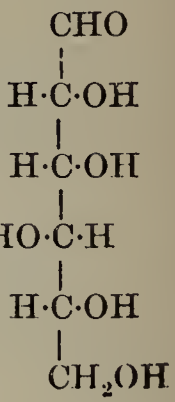
$\underline{(6^1)}$



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{CHO} \end{array}$$

or when rotated 180°

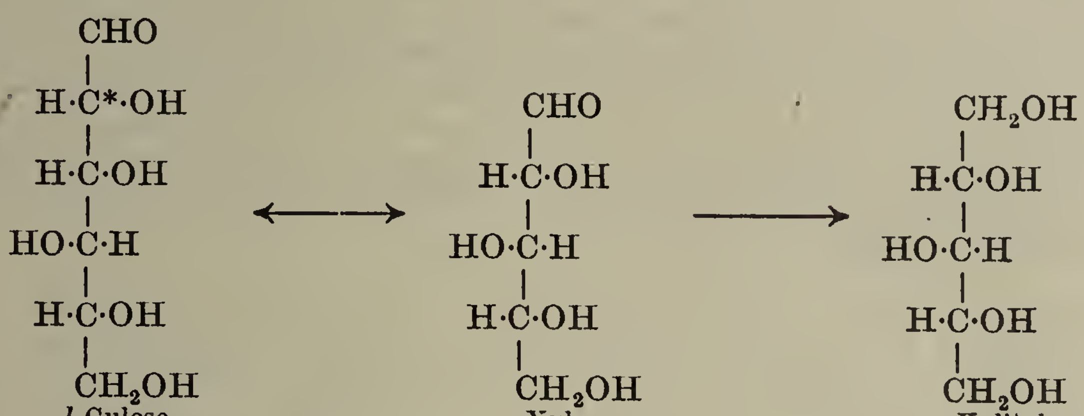
(6^1)



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{HO\cdot C\cdot H} \\ | \\ \mathrm{H\cdot C\cdot OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

Remembering that, according to diagram IV (p. 707), it is possible to obtain *l*-glucose from *l*-arabinose, and, according to diagram V, *l*-gulose from xylose, then the pentoses mentioned must have the space-formulæ which can be derived for formulæ (5^1) and (6^1) by omitting the first of the C*-atoms, by which the structure becomes asymmetric :

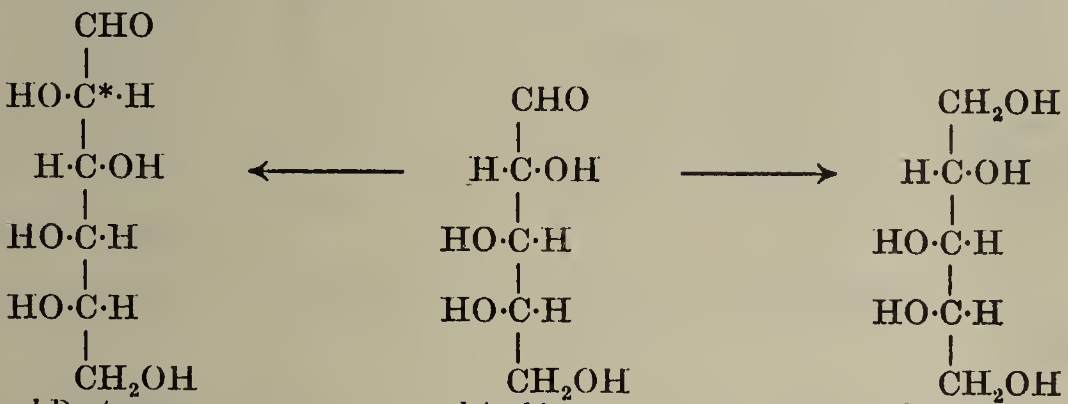
(6^1)



$$\begin{array}{c}\text{CHO}\\ \mid\\ \text{H·C*·OH}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{CH}_2\text{OH}\end{array} \longleftrightarrow \begin{array}{c}\text{CHO}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{CH}_2\text{OH}\end{array} \longrightarrow \begin{array}{c}\text{CH}_2\text{OH}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{CH}_2\text{OH}\end{array}$$

l-Gulose. Xylose. Xylitol.

(5^1)

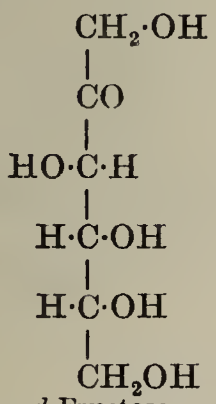


$$\begin{array}{c}\text{CHO}\\ \mid\\ \text{HO·C*·H}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{CH}_2\text{OH}\end{array} \longleftarrow \begin{array}{c}\text{CHO}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{CH}_2\text{OH}\end{array} \longrightarrow \begin{array}{c}\text{CH}_2\text{OH}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{CH}_2\text{OH}\end{array}$$

l-Dextrose. *l*-Arabinose. *l*-Arabitol.

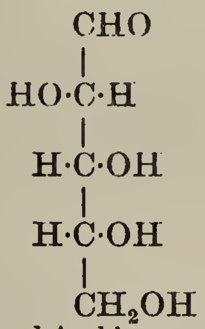
It is at once seen that the aldopentose corresponding with formula (6^1) must, by reduction, yield an inactive pentitol, xylitol (p. 703)—through an internal compensation. Similarly, the pentose with formula (5^1) changes to an optically active pentitol—*l*-arabitol (p. 703). In this manner is fixed not only the configuration for xylitol and xylose, *l*-arabitol and *l*-arabinose, but it is also demonstrated that *l*-gulose, from xylose, has the formula (6^1), and *l*-dextrose, synthesized from *l*-arabinose, the space-formula (5^1). (8^1) is the stereoisomeric formula of space-formula (6^1), which, therefore, belongs to *d*-gulose. Formula (7^1) corresponds with space-formula (5^1), and hence it belongs to *d*-glucose. From all this it would follow that *d*- and *l*-mannoses have formulæ (2^1) and (1^1), which facts confirm that *d*-glucose and *d*-mannose on the one hand, and *l*-glucose and *l*-mannose on the other, pass into the same glucosazone—*i.e.* they differ only in the configuration at one asymmetric C-atom.

When it is remembered that *d*-fructose, by reduction, yields a mixture of *d*-mannitol and *d*-sorbitol, and *d*-glucosazone on treatment with phenylhydrazine, it will be recognized that both it and its corresponding *d*-arabinose must have the space-formulæ :



$$\begin{array}{c}\text{CH}_2\text{·OH}\\ \mid\\ \text{CO}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{CH}_2\text{OH}\end{array}$$

d-Fructose.



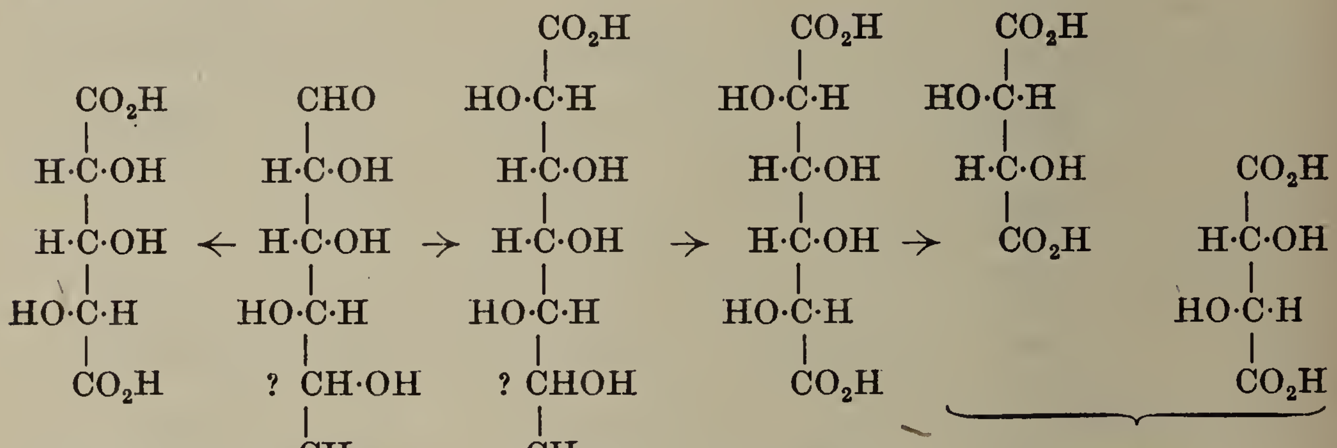
$$\begin{array}{c}\text{CHO}\\ \mid\\ \text{HO·C·H}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{H·C·OH}\\ \mid\\ \text{CH}_2\text{OH}\end{array}$$

d-Arabinose.

The configurations of other ketoses, such as tagatose and sorbose (p. 699), can similarly be derived.

Derivation of the Configuration of d-*Tartaric Acid* *

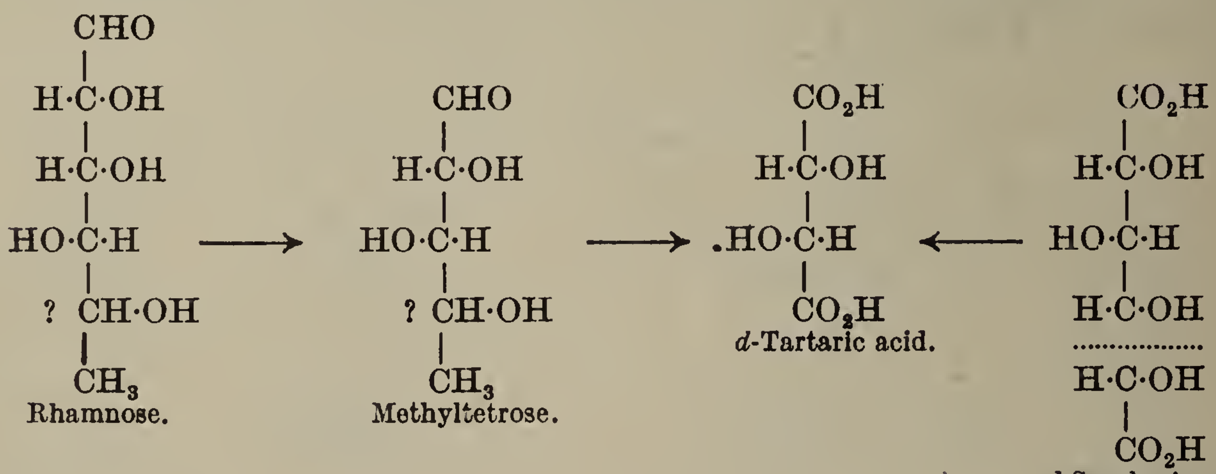
The configuration of *d*-tartaric acid is evident, according to E. Fischer, from its production in the oxidation of *d*-saccharic acid. The formula of the latter has been previously deduced above. It is in harmony, therefore, with its formation in the oxidation of methyltetrose (p. 651), a decomposition product of rhamnose. The latter, when oxidized, passes into *l*-trihydroxyglutaric acid. The α-rhamnohexonic acid, obtained from the rhamnose by the hydrocyanic acid addition, yields mucic acid on oxidation, and the latter, on similar treatment, changes to racemic acid. Assuming that the methyl group of rhamnose is eliminated in the oxidation of rhamnohexonic acid, rhamnose would have the following configuration-formula :



l-Trihydroxyglutaric acid. Rhamnose. α-Rhamnosecarboxylic acid. Mucic acid. Racemic acid.

This assumption has been proved through the behaviour of the stereoisomeric β-rhamnohexonic acid, which results on heating α-rhamnohexonic acid to 140° with pyridine. All experiences go to show that the two stereoisomeric rhamnohexonic acids only differ in the arrangement or position of the carboxyl group in direct union with the asymmetric carbon atom. Had the methyl group not been split off in the oxidation, but merely changed to carboxyl, then α- and β-rhamnohexonic acids would have yielded the same mucic acid, because the asymmetric C-atom linked to carboxyl in α- and β-rhamnohexonic acid, that caused the difference in the two acids, would have been oxidized to carboxyl. β-Rhamnohexonic acid, however, oxidizes to *l*-talomucic acid, which justifies the preceding assumption, and consequently proves the configuration, even to the position of the asymmetric carbon atom linked to methyl.

Wohl's procedure permits of the conversion of rhamnose into methyltetrose, which is oxidized to *d*-tartaric acid by nitric acid. Hence, we may suppose that here the methyl group is split off as in the case of the oxidation of rhamnose to *l*-trihydroxyglutaric acid, and of α-rhamnohexonic acid to mucic acid. This then demonstrates the configuration of *d*-tartaric acid (Ber. **29**, 1377) :



Rhamnose. Methyltetrose. *d*-Tartaric acid. *d*-Saccharic acid.

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* See also Kurt Hoesch, Sonderhett, Ber. **54**, 334.

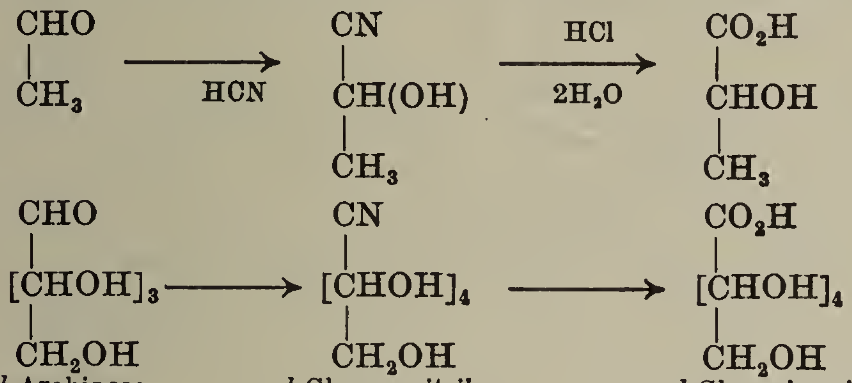
4. HEXAKETONES

Oxalylbisacetylacetone, $(CH_3CO)_2CHCO{\cdot}CO{\cdot}CH(COCH_3)_2$, is the parent substance of *dicyanobisacetylacetone*, $\alpha\alpha_1$-tetraacetyl-$\beta\beta_1$-diiminobutane, $(CH_3CO)CHC(NH){\cdot}C(NH){\cdot}CH(COCH_3)_2$, m.p. 147°, which is prepared from dicyanomonoacetylacetone (p. 652), acetylacetone, and a little alcoholate. Even when boiled in water it is changed into a carbocyclic derivative (Ann. **332**, 146).

5. POLYHYDROXYMONOCARBOXYLIC ACIDS

A. PENTAHYDROXYCARBOXYLIC ACIDS

These acids are produced (1) by the oxidation of the alcohols and aldoses corresponding with them, by means of chlorine or bromine water (Ber. **32**, 2273) with nitric acid (D 1·2) (Ber. **54**, 456) or with barium hypoiodite (J. Biol. Chem. **72**, 809); (2) by the reduction of the corresponding aldehydo-acids and lactones of dicarboxylic acids; synthetically, from the aldopentoses (arabinose, rhamnose, p. 672) by means of HCN, etc. This is analogous to the synthesis of glycollic acid from formaldehyde, and lactic acid from acetaldehyde:



$$\begin{array}{l} CHO \\ | \\ CH_3 \end{array} \xrightarrow[HCN]{} \begin{array}{l} CN \\ | \\ CH(OH) \\ | \\ CH_3 \end{array} \xrightarrow[2H_2O]{HCl} \begin{array}{l} CO_2H \\ | \\ CHOH \\ | \\ CH_3 \end{array}$$

$$\begin{array}{l} CHO \\ | \\ [CHOH]_3 \\ | \\ CH_2OH \end{array} \longrightarrow \begin{array}{l} CN \\ | \\ [CHOH]_4 \\ | \\ CH_2OH \end{array} \longrightarrow \begin{array}{l} CO_2H \\ | \\ [CHOH]_4 \\ | \\ CH_2OH \end{array}$$

l-Arabinose. *l*-Glucononitrile. *l*-Gluconic acid. (*l*-Arabinosecarboxylic acid.)

Behaviour.—(1) Being γ- and δ-hydroxyl-derivatives, nearly all of these acids are very unstable when in a free condition. They lose water readily and pass into *lactones* (p. 424):

$$C_6H_{12}O_7 \xrightarrow{-H_2O} C_6H_{10}O_6.$$

Hudson's Rule.—Hudson (J.A.C.S. **32**, 338) has pointed out a relationship between the direction of rotation of a lactone and the position of the lactone ring. If the formula of the lactone is written from above downwards, the carboxyl group at the top, and using the projection formulæ already given (p. 704), the direction of rotation of the compound is given by the position of the lactone ring to the right or left of the formula. Contrariwise, from the direction of rotation, the position of the lactone ring can be deduced.

(2) The capacity of the lactones, but not the acids themselves, to pass into the corresponding aldohexoses by combination with two atoms of hydrogen (E. Fischer), is of great importance in the synthesis of the aldoses (p. 683):

$$\underset{d\text{-Gluconolactone.}}{C_6H_{10}O_6} \xrightarrow{2H} \underset{d\text{-Glucose.}}{C_6H_{12}O_6}.$$

(3) These acids, when acted on with phenylhydrazine, form characteristic crystalline *phenylhydrazides*, $C_5H_{11}O_5{\cdot}CO{\cdot}N_2H_2C_6H_5$ (Ber.

22, 2728). These are decomposed into their components when boiled with alkalis. They are distinguished from the hydrazones of the aldehydes and ketones by the reddish-violet coloration produced upon mixing them with concentrated sulphuric acid and a drop of ferric chloride.

(4) Heated to 130–150° with quinoline or pyridine a geometric rearrangement ensues, restricted to the asymmetric carbon atom in union with the carboxyl (*Epimeric change*) (*cf.* the inter-transformation of stereomeric hexoses under the influence of alkali, p. 687). It is a reversible reaction, and therefore yields a mixture of both stereoisomers, *e.g.* (Ber. **27**, 3193):

$$\begin{array}{lcl} d\text{-Gluconic acid} & \rightleftarrows & d\text{-Mannonic acid.} \\ l\text{-Gulonic acid} & \rightleftarrows & l\text{-Idonic acid.} \\ d\text{-Galactonic acid} & \rightleftarrows & d\text{-Talonic acid.} \end{array}$$

(5) These acids are reduced to lactones of the γ-monohydroxycarboxylic acids (p. 424), if they are heated with hydriodic acid.

(6) Oxidation of the hexonic acids or their lactones with hydrogen peroxide and ferric acetate, causes degradation to the pentoses (see p. 673).

Isomerism.—Spacial isomers of pentahydroxy-*n.*-caproic acid are as numerous, according to theory, as the aldohexoses (p. 704), *i.e.* sixteen optically active and eight *dl*-modifications, which are inactive.

Mannonic acid, $C_5H_6(OH)_5{\cdot}CO_2H$. The syrup-like acids—*d*-, *l*-, and *dl*-mannonic acids—yield the corresponding dibasic mannosaccharic acids on oxidation (p. 717). They change to lactones on the evaporation of their solutions; these by reduction yield the mannoses and mannitols. *dl*-Mannitol is identical with α-acritol, the reduction product of synthetic α-acrose or *dl*-fructose. As *dl*-mannitol or α-acritol, when oxidized, yields *dl*-mannose, and the latter by similar treatment becomes converted into *dl*-mannonic acid, which can be split into *d*-mannonic acid and *l*-mannonic acid, the complete synthesis of all bodies of the mannitol series can be realized through these reactions (p. 701):

$$\begin{tikzcd}
 & d\text{-Mannitol} & d\text{-Mannose} \arrow[l] & d\text{-Mannonolactone} \arrow[l] & \\
 & & & d\text{-Mannonic acid} \arrow[u] \arrow[r] & \begin{matrix} d\text{-Mannosaccharic} \\ \text{acid} \end{matrix} \\
\begin{matrix} \alpha\text{-Acrose} \\ dl\text{-Fructose} \end{matrix} \arrow[r] & \begin{matrix} \alpha\text{-Acritol} \\ dl\text{-Mannitol} \end{matrix} \arrow[r] & dl\text{-Mannose} \arrow[r] & dl\text{-Mannonic acid} \arrow[u] \arrow[d] \arrow[r] & \begin{matrix} dl\text{-Mannosaccharic} \\ \text{acid} \end{matrix} \\
 & & & l\text{-Mannonic acid} \arrow[d] \arrow[r] & \begin{matrix} l\text{-Mannosaccharic} \\ \text{acid} \end{matrix} \\
 & l\text{-Mannitol} & l\text{-Mannose} \arrow[l] & l\text{-Mannonolactone.} \arrow[l] &
\end{tikzcd}$$

d-*Mannonolactone*, $C_6H_{10}O_6$, m.p. 149–153° $[\alpha]_D = +\ 53{\cdot}8°$
l-*Mannonolactone*, „ 140–150° $[\alpha]_D = -\ 53{\cdot}2°$
dl-*Mannonolactone*, $(C_6H_{10}O_6)_2$, „ 149–155°.

d- and l-*Mannonic acid phenylhydrazides*, $C_6H_{11}O_6(N_2H_2{\cdot}C_6H_5)$, m.p. 215°.

dl-*Mannonic acid phenylhydrazide*, m.p. about 230° when rapidly heated. The hydrazides are converted into the acids on boiling with barium hydroxide solution (Ber. **22**, 3221), a reaction which is well adapted for the purification of the acids. d- and l-*Methylene mannonic lactone*, $(C_6H_8O_6(CH_2)$, m.p. 206° (Ann. **310**, 181).

A very important feature is the partial conversion of *d*- and *l*-mannonic acids into *d*- and *l*- gluconic acids on heating the former to 140° with quinoline, referred to in (4) (p. 712).

This method of preparing *d*- and *l*-gluconic acids shows the genetic connection existing between *d*- and *l*-glucose and the mannitol series, and thereby renders possible the synthesis of glucose.

The formation of l-mannonic acid or *l*-arabinosecarboxylic acid (together with *l*-gluconic acid) from *l*-arabinose by means of hydrocyanic acid, constitutes one of the transitions which allows of the synthesis of aldohexoses from aldopentoses :

$$l\text{-Arabinose}\begin{cases} l\text{-Mannonic acid} \longrightarrow l\text{-Mannonolactone} \longrightarrow l\text{-Mannose} \\ l\text{-Gluconic acid} \longrightarrow l\text{-Gluconolactone} \longrightarrow l\text{-Glucose.} \end{cases}$$

Gluconic acid, $CH_2OH[CHOH]_4CO_2H$, is known in the *d*-, *l*-, and *dl*-modifications (Ber. **23,** 801, 2624 : **24,** 1840) (space formula, see p. 705).

1. The lactones of these three acids yield the corresponding glucose on reduction.

2. By oxidation they yield the corresponding dibasic saccharic acids.

3. When heated to 140° with quinoline they undergo epimeric change (p. 712) with the partial formation of the corresponding mannonic acid.

d- and l-*Phenylhydrazides*, $C_6H_{11}O_6(N_2H_2{\cdot}C_6H_5)$, m.p. about 200° when they are rapidly heated ; dl-*phenylhydrazide*, m.p. 190°.

d-**Gluconic acid** is formed from saccharose, maltose, dextrin starch, or particularly readily from glucose, by oxidation with chlorine or bromine water (Ber. **17,** 1298). It is also obtained from glucose by oxidation with nitric acid (D 1·2) (Ber. **54,** 456) or barium hypoiodite (J. Biol. Chem. **72,** 809). It is also formed from mannonic acid by epimeric change (see above).

Gluconic acid forms a syrup which, when evaporated or upon standing, changes in part to its crystalline *lactone*, $C_6H_{10}O_6$, m.p. 130–135°. Sodium amalgam reduces it to *d*-glucose or grape sugar (Ber. **23,** 804).

Its *barium* salt crystallizes with three molecules of water ; *calcium salt* with one. The acid is dextrorotatory. On the conversion into *d*-arabinose by oxidation with H_2O_2, see p. 673.

Pentaacetyl gluconoitrile, $C_5H_6(O{\cdot}C_2H_3O)_5CN$ (Ber. **26,** 730). *Dimethylene gluconic acid*, $C_6H_8O_7(:CH_2)_2$, m.p. 220°, is prepared from *d*-gluconic acid and formaldehyde (Ann. **292,** 31 : **310,** 181).

l-**Gluconic acid** is formed (1) from *l*-mannonic acid by epimeric change (p. 712) and (2) together with *l*-mannonic acid from *l*-arabinose by aid of HNC.

dl-**Gluconic acid** is obtained from a mixture of *d*- and *l*-gluconic acids. Its *calcium* salt, which dissolves with difficulty, is obtained, like calcium racemate, by mixing solutions of *d*- and *l*-calcium gluconates.

Gulonic acid, $CH_2OH[CHOH]_4CO_2H$, is known in three forms, which yield the corresponding saccharic acids on oxidation and the corresponding guloses on reduction of their lactones.

d-**Gulonic acid** is obtained by the reduction of glycuronic acid (p. 716) or of saccharic acid. Its *lactone*, m.p. 181°, $[\alpha]_D + 55{\cdot}1°$, yields *d*-xylose on oxidation with hydrogen peroxide and ferric acetate (p. 673). *Phenylhydrazide*, m.p. 148° (Ber. **24,** 526).

l-**Gulonic acid**, *xylosecarboxylic acid*, results when xylose is acted on with HNC. This reaction unites also the aldopentoses with the aldohexoses. *l*-Idonic acid is produced simultaneously, and when heated with pyridine changes partially to *l*-gulonic acid. l-*Gulonic lactone*, m.p. 185°, yields *l*-xylose when oxidized with H_2O_2 (p. 673); *phenylhydrazide*, m.p. 148° (Ber. **23**, 2628: **24**, 528).

dl-**Gulonic acid** readily changes into its *lactone*, which by crystallization splits into *d*- and *l*-gulonolactone. *Calcium* dl-*gulonate* dissolves with more difficulty than calcium *d*- and *l*-gulonate; *phenylhydrazide*, m.p. 154° (Ber. **25**, 1025).

l-**Idonic acid** is formed together with *l*-gulonic acid from xylose, and is separated by means of its brucine salt from the mother liquor of *l*-gulonolactone. Heated with pyridine to 140°, it changes in part to *l*-gulonic acid, and vice versa. *l*-Idose is its reduction product (p. 697). *d*-Idonic acid, obtained from *d*-gulonic acid by means of pyridine, yields *d*-idose on reduction (Ber. **28**, 1975).

dl-**Galactonic acid** results in the reduction of ethyl mucate and also of the lactone of mucic acid; *lactone*, m.p. 122–125°; *phenylhydrazide*, m.p. 205°. This acid can be resolved by means of its strychnine salt into the *l*-salt, which is more easily soluble in alcohol, and the *d*-salt, which dissolves with more difficulty (Ber. **25**, 1256).

d-**Galactonic acid**, *lactonic acid*, $CH_2OH[CHOH]_4CO_2H$, is produced from lactose, *d*-galactose, and gum arabic by the action of bromine water or nitric acid (Ber. **54**, 456) and together with *d*-talonic acid, from *d*-lyxose cyanohydrin by hydrolysis (Ber. **33**, 2146). It can be converted into *d*-talonic acid by epimerization. It is converted into mucic acid by oxidation with nitric acid (p. 718). It crystallizes, and at 100°, yields d-*galactonic lactone*, $C_6H_{10}O_6$, m.p. 91° $[\alpha]_D$ − 70·8°, which unites with water of crystallization to form $C_6H_{10}O_6 + H_2O$, m.p. 64° (Ann. **271**, 83). Acetyl chloride produces *triacetylchlorogalactonic lactone*, $C_6H_6O_2(OCOCH_3)_3Cl$, m.p. 98° (Ber. **35**, 943). Reduction converts the lactone into *d*-galactose (p. 697); *calcium salt*, $(C_6H_{11}O_7)_2Ca + 5H_2O$; *phenylhydrazide*, m.p. 200–205°; *amide*, m.p. 175°; *anilide*, m.p. 210° (Ber. **28**, R. 606).

Dimethylene galactonic acid, $C_5H_7O_5(CH_2)_2CO_2H$, m.p. 136° (Ann. **310**, 181). *Pentaacetyl*-d-*galactonic nitrile*, b.p. 135°, is formed from *d*-galactose oxime and acetic anhydride, and yields, with silver oxide and ammonia, the acetamide compound of lyxose (p. 673).

d-**Talonic acid**, $CH_2OH[CHOH]_4CO_2H$, results together with hydroxymethylene pyromucic acid on heating *d*-galactonic acid with pyridine or quinoline to 140–150°. Conversely, *d*-galactonic acid is obtained from *d*-talonic acid by the same treatment (Ber. **27**, 1526). Reduction changes it to *d*-talose (p. 697).

α-**Rhamnosecarboxylic acid**, $CH_3[CHOH]_5CO_2H$, is formed from rhamnose (see *iso*Dulcitol, p. 675) with HNC, etc.; *lactone*, $C_7H_{12}O_6$, m.p. 162–168° $[\alpha]_D$ + 86° (Ber. **21**, 2173); *phenylhydrazide*, $C_7H_{13}O_6{\cdot}N_2H_2C_6H_5$, m.p. about 210° (Ber. **22**, 2733). When heated with hydrochloric acid and phosphorus it is reduced to *n*-heptylic acid, $C_7H_{14}O_3$; sodium amalgam reduces the lactone to methylhexose (p. 698) (Ber. **23**, 936). Oxidation produces mucic acid (Ber. **27**, 384).

β-**Rhamnosecarboxylic acid** is formed when the α-compound is heated to 150–155° with pyridine; *lactone*, m.p. 134–138° $[\alpha]_D$ + 43·3°; *phenylhydrazide*, m.p. 170°. Oxidation converts the β-acid into *l*-talomucic acid (p. 719).

Chitonic acid, which is produced from chitose (p. 699) and bromine water, and **chitaric acid**, $C_6H_{10}O_6$, prepared from *d*-glucaminic acid (see above) and nitrous acid are probably stereomeric *trihydroxymethyltetrahydrofurancarboxylic acids*, $HOCH_2{\cdot}CH(O)CH(OH)CH(OH)CHCO_2H$, since acetic anhydride converts it into the acetyl derivative of hydroxymethylpyromucic acid, $CH_2CO{\cdot}O{\cdot}CH_2{\cdot}C(O):CH{\cdot}CH:CCO_2H$ (Vol. II); Ber. **36**, 2587). Oxidation with H_2O_2 and ferrous sulphate degrades chitonic acid into *d*-arabinose or *d*-ribose (p. 675) (Ber. **35**, 4016).

Glucosaminic acid, *α-amino-βγδε-tetrahydroxycaproic acid*, $HOCH_2[CHOH]_3CH(NH_2)CO_2H$, is known in *d*-, *l*-, and *dl*-forms. *d*- and *l*-Glucosaminic acids are prepared from *d*- and *l*-arabinosimine (p. 699), hydrocyanic and hydrochloric acids, and unite to form the less soluble *dl*-acid. *d*-Glucosaminic acid is also prepared from *d*-glucosamine and bromine water. Alcohol and hydrochloric acid convert it into a lactone-like syrup, which, on reduction with sodium amalgam, regenerates *d*-glucosamine. Reduction with hydriodic acid produces α-aminocaproic acid; with nitrous acid it forms chitaric acid (see above). It yields α- and *β-aminoglucoheptonic acids*, $CH_2OH[CHOH]_3CH(NH_2)CHOHCO_2H$, with hydrocyanic and hydrochloric acids (Ber. **36**, 27, 618).

Galaheptosaminic acid, $CH_2OH[CHOH]_4CH(NH)_2CO_2H$, m.p. 240° with decomposition, is prepared from galactosimine (p. 699) and hydrocyanic and hydrochloric acids (Ber. **35**, 3801).

B. HEXOSECARBOXYLIC ACIDS, HEXAHYDROXYMONOCARBOXYLIC ACIDS

Acids of this kind have been obtained from *d*-glucose, *d*-mannose, *d*-galactose, and *d*-fructose by the addition of hydrocyanic acid, and the subsequent saponification of the nitrile with hydrochloric acid.

(1) ***d*-Mannosecarboxylic acid**, d-*mannoheptonic acid*, $CH_2OH{\cdot}[CHOH]_5{\cdot}CO_2H$, is obtained from *d*-mannose (Ann. **272**, 197); *phenylhydrazide*, m.p. about 220° (decomp.); *lactone*, m.p. 149° $[\alpha]_D - 74{\cdot}2°$. Sodium amalgam reduces the lactone to *d*-mannoheptose, $C_7H_{14}O_7$, and then to the heptahydric alcohol perseitol, $C_7H_{16}O_7$ (Ber. **23**, 936, 2226). Hydriodic acid reduces the acid to heptolactone and heptylic acid (see above and Ber. **22**, 370). When oxidized it yields *l*-pentahydroxypimelic acid (Ann. **272**, 194).

***l*-Mannosecarboxylic acid** is obtained from *l*-mannose; *phenylhydrazide*, m.p. about 220°; *lactone*, m.p. 154°.

***dl*-Mannosecarboxylic acid** is formed from *d*- and *l*-mannosecarboxylic acids, as well as from *dl*-mannose (Ann. **272**, 184).

(2) **α-*d*-Glucosecarboxylic acid**, *α-d-glucoheptonic acid*, $CH_2OH[CHOH]_5{\cdot}CO_2H$, is formed (1) together with the *β*-acid from *d*-glucose; (2) on heating the *β*-acid to 140° with pyridine; (3) by the hydrolysis of lactose- and maltose-carboxylic acids (p. 726) (Ann. **272**, 200); *lactone*, m.p. 140–145° $[\alpha]_D - 56°$. Hydriodic acid reduces it to heptolactone and normal heptylic acid. Sodium amalgam reduces the lactone to *d*-glucoheptose. *Dimethylene-α-glucoheptonic lactone*, $C_7H_8(CH_2)_2O_7$, m.p. 280°. The acid, when oxidized, is converted into inactive pentahydroxypimelic acid (p. 719); *phenylhydrazide*, m.p. 171° (Ber. **19**, 1916: **23**, 936: space-formula, Ann. **270**, 65).

***β-d*-Glucosecarboxylic acid** is formed together with the α-acid from dextrose; *phenylhydrazide*, m.p. 151°; *lactone*, m.p. 151°, and yields *β*- *d*-glucoheptose on reduction (p. 700). *Dimethylene-β-glucoheptonic lactone*, m.p. 230° (Ann. **299**, 328: **310**, 181).

α-*d*-Galactosecarboxylic acid, *α-galaheptonic acid*, $CH_2OH[CHOH]_5CO_2H$, m.p. 145°, is produced together with *β-galaheptonic acid* from galactose; *lactone*, m.p. 150°. Sodium amalgam changes it into α-galaheptose (p. 700). When oxidized it yields carboxy-*d*-galactonic acid (p. 719) (Ann. **288**, 39).

***d*-Fructosecarboxylic acid**, $CH_2OH{\cdot}[CHOH]_3C(OH)(CO_2H)CH_2OH$, is obtained from fructose by the action of hydrocyanic acid. It yields tetrahydroxybutanetricarboxylic acid when it is oxidized. Its *lactone*, m.p. 130°; when reduced with sodium amalgam two aldoheptoses with branched C-chains result (Ber. **23**, 937). Reduction with hydriodic acid forms heptolactone and a heptoic acid, $C_7H_{14}O_2$. The latter is identical with methyl-*n*.-butylacetic acid (p. 210). Hence it is evident that lævulose is a ketone-alcohol (Kiliani, Ber. **19**, 1914: **23**, 451: **24**, 348).

C. ALDOHEPTOSECARBOXYLIC ACIDS, HEPTAHYDROXYCARBOXYLIC ACIDS

***d*-Mannooctonic acid**, $CH_2OH{\cdot}[CHOH]_6CO_2H$, has been obtained from *d*-mannoheptose (p. 700); *hydrazide*, m.p. 243°; *lactone*, m.p. about 168°, has a neutral reaction, and a sweet taste. By reduction it forms *d*-mannooctose (p. 700).

α- and *β*-Glucooctonolactone, m.p. 145° and 186° (Ann. **270**, 93).

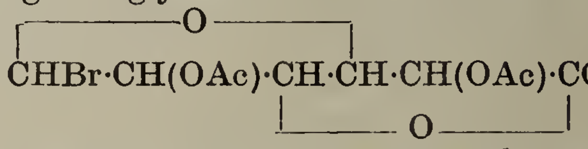
α-Galaoctonolactone, from α-galaheptose (Ann. **288**, 149).

D. ALDOOCTOSECARBOXYLIC ACIDS, OCTOHYDROXYCARBOXYLIC ACIDS

d-**Mannonononic acid**, $CH_2OH[CHOH]_7CO_2H$, has been obtained from *d*-mannooctose; *hydrazide*, m.p. 254°; *lactone*, m.p. 176° $[\alpha]_D - 41°$. When reduced it forms *d*-mannononose (p. 700).

6. TETRAHYDROXY- AND PENTAHYDROXY-ALDEHYDE ACIDS

d-**Glucuronic acid** (*glycuronic acid*), $CHO(CHOH)_4CO_2H$, is obtained by decomposing euxanthic acid (Vol. II) on boiling with dilute sulphuric acid. Various glucoside-like compounds of glycuronic acid with camphor, borneol, chloral, phenol, and different other bodies (Ber. **19**, 2919, R. 762) occur in urine after the introduction of these compounds into the animal organism. In this change the substances mentioned combine with the aldehyde group of dextrose, the primary alcohol group of which is then oxidized. Boiling acids decompose them into their components.

Synthetically, such conjugated glycuronic acids can also be obtained from *diacetylbromoglycurolactone*,  $\overbrace{\mathrm{CHBr\cdot CH(OAc)\cdot}\underbrace{\mathrm{CH\cdot CH\cdot CH(OAc)\cdot CO}}_{\mathrm{O}}}^{\mathrm{O}}$, m.p. 90°, the product of reaction between glycuronic lactone and acetyl bromide which react with euxanthone (Vol. II) or phenol (Vol. II) and sodium alcoholate, to give rise to euxanthic or phenol glycuronic acids (C. 1905, I. 1086). Glycuronic acid can be identified in animal secretions by the blue-coloured substance, soluble in ether, which is formed with β-naphthoresorcinol and hydrochloric acid (Ber. **41**, 1788).

Glycuronic acid is usually met with as a syrup, but can be obtained crystalline with difficulty (Ber. **58**, 1990). It then melts at 157°, and shows mutarotation in aqueous solution from $+ 11{\cdot}7°$ to $+ 36{\cdot}26°$. Its *lactone*, glucurone, melts at 175°. (Derivatives of the lactone, see Ber. **33**, 3315.)

Bromine water oxidizes it to *d*-saccharic acid. When saccharic acid is reduced glycuronic acid results (Ber. **23**, 937), and by further reduction *d*-gluconic acid (p. 713) is formed (Ber. **24**, 525). The acid unites with potassium cyanide to form the half-nitrile of α-glucopentahydroxypimelic acid (p. 719); with three molecules of phenylhydrazine to form an *osazone*, m.p. 200–205°; and with urea, accompanied by loss of water (C. 1905, I. 1084).

Urochloralic acid, $C_7H_{11}Cl_3O_7$, m.p. 142°, decomposes with water absorption on boiling with dilute hydrochloric or sulphuric acid into glycuronic acid and trichloroethyl alcohol (p. 144). *Urobutylchloralic acid*, $C_{10}H_{15}Cl_3O_7$, decomposes, like the preceding body, into glycuronic acid and ααβ-trichlorobutyl alcohol (p. 146).

Galacturonic acid, the corresponding compound of the galactose series, is an important constituent of the pectin material of plants.

Aldehydogalactonic acid, $COH[CHOH]_5CO_2H$, is obtained from *d*-galactose carboxylic acid, and may be converted into carboxygalactonic acid (p. 719).

7. MONOKETOTETRAHYDROXYCARBOXYLIC ACIDS

Hydroxygluconic acid, $HOCH_2{\cdot}CO[CHOH]_3CO_2H$, is formed, together with *d*-arabinose, when calcium gluconate is oxidized; also by bacterial action (Ber. **32**, 2269).

8. POLYHYDROXYDICARBOXYLIC ACIDS

A. TETRAHYDROXYDICARBOXYLIC ACIDS

These are obtained by the oxidation of various carbohydrates with nitric acid, and are readily prepared from the corresponding monocarboxylic acids (p. 711) upon oxidation with nitric acid. Mannosaccharic acid, the saccharic acids, and the mucic acids are the most important representatives of the series. Gluconic acid yields saccharic acid, galactonic acid mucic acid, and mannonic acid mannosaccharic acid. Their lactones, by very careful reduction, can be converted into tetrahydroxyaldehydocarboxylic acids and pentahydroxycarboxylic acids. When reduced by HI and phosphorus the preceding acids are converted into normal adipic acid (p. 561), hence all of them must be considered as normal stereoisomeric tetrahydroxyadipic acids. Theoretically, ten simple and four racemic modifications are possible, as in the case of the *n.*-hexitols (p. 704). All the tetrahydroxyadipic acids, when heated with hydrochloric or hydrobromic acid, change more or less readily to dehydromucic acid (Ber. **24**, 2140).

(1) **Mannosaccharic acid,** $CO_2H[CHOH]_4CO_2H$, is known in three modifications (configurations, p. 704), which pass into double lactones when they are liberated from their salts. They also result upon oxidizing the three mannonic acids with nitric acid (p. 712).

dl-*Mannosaccharolactone*, $C_6H_6O_6$, m.p. 190° (decomp.), is formed by the union of *d*- and *l*-mannosaccharolactones and also from *dl*-mannonolactone; *diamide*, m.p. 184°; *dihydrazide*, m.p. 220–225° (Ber. **24**, 545).

d-*Mannosaccharolactone*, $C_6H_6O_6 + 2H_2O$, m.p. 181° (anhydrous) $[\alpha]_D$ + 204·8°, is produced when *d*-mannitol, *d*-mannose, and *d*-mannonic acid are oxidized with nitric acid; *diamide*, m.p. 189°; *dihydrazide*, m.p. 212° (Ber. **24**, 544).

l-*Mannosaccharolactone, metasaccharic acid*, $C_6H_6O_6 + 2H_2O$, m.p. 68° (anhydrous), 180°, is produced when *l*-mannonic acid and the lactone of *l*-arabinosecarboxylic acid are oxidized (Ber. **20**, 341, 2713); *diamide*, m.p. 190°; *dihydrazide*, m.p. 213°. *Diacetyl*-l-*mannosaccharolactone*, m.p. 155° (Ber. **21**, 1422: **22**, 525: **24**, 541).

(2) *d*- and *l*-**Idosaccharic acids** are syrups. They are obtained by oxidizing the corresponding idonic acid (p. 714) (configurations, p. 704).

(3) **Saccharic acid,** $CO_2H[CHOH]_4CO_2H$, exists in three modifications (configurations, p. 705).

dl-**Saccharic acid** is formed by the oxidation of *dl*-gluconic acid. Its monopotassium salt is formed on mixing solutions of equal quantities of the *d*- and *l*-salt; *dihydrazide*, m.p. 210° (Ber. **23**, 2622).

Ordinary, or *d*-**Saccharic acid,** results in the oxidation of sucrose (Ber. **21**, R. 472), *d*-glucose (grape sugar), *d*-gluconic acid and *d*-gluconic lactone (Ber. **24**, 521), and many carbohydrates with nitric acid; also from the action of bromine water on glucuronic acid (p. 716).

It forms a deliquescent mass, readily soluble in alcohol, which is dextrorotatory, $[\alpha]_D$ (Equilibrium, acid + lactone) + 22·5°, and gradually solidifies to a mass of crystals of the lactonic acid $C_6H_8O_7$, m.p. 131°, $[\alpha]_D$ + 37·9°. Sodium amalgam reduces it to glycuronic acid and hydriodic acid to adipic acid. On oxidation, *d*-saccharic acid yields, together with oxalic acid, 61% of *d*-tartaric acid and

38% of racemic acid (Ann. **429,** 152). The diamide of saccharic acid is degraded by bromine and alkali to the dialdehyde of *l*-tartaric acid (Ber. **54,** 2651).

The *hydrogen potassium salt*, $C_6H_9O_8K$, and the *ammonium salt*, $C_6H_9O_8(NH_4)$, dissolve with difficulty in cold water; *diethyl ester* is crystalline; *ethyl ester tetraacetate*, m.p. 61°. Acetyl chloride, acting on free saccharic acid, converts it into the *lactone* of *diacetylsaccharic acid*, $C_6H_4(O{\cdot}C_2H_3O)_2O_4$, m.p. 188°. *Monomethylenesaccharic acid* (Ann. **292,** 40). The *diamide* is a white powder; *dihydrazide*, m.p. 210° (decomp.) (Ber. **21,** R. 186).

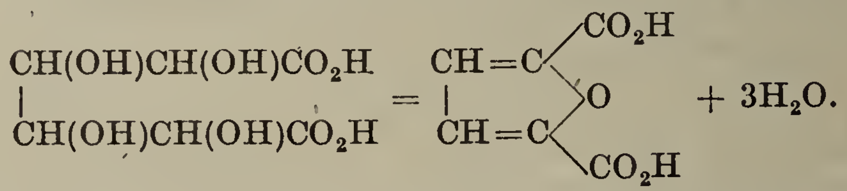
l-**Saccharic acid** is obtained upon oxidizing *l*-gluconic acid with nitric acid. It is quite similar to *d*-saccharic acid, but is lævorotatory. It also forms a *dihydrazide*, m.p. 214°.

(4) **Mucic acid,** $CO_2H[CHOH]_4CO_2H$, m.p. 210° (decomp.), corresponds in constitution with dulcitol, and possesses the space-formula No. 7 (p. 705), one of the two theoretically possible forms of tetrahydroxyadipic acid, optically inactive through internal compensation. This is supported by its oxidation to racemic acid, and its formation by oxidation from α-rhamnosecarboxylic acid (p. 714) (Ber. **27,** 396).

It is also obtained in the oxidation of dulcitol, lactose (Preparation, Ann. **227,** 224), *d*- and *l*-galactose, *d*- and *l*-galactonic acid, and nearly all the gum varieties.

It is a white crystalline powder, almost insoluble in cold water and alcohol. When boiled for some time with water it passes into a readily soluble lactonic acid, $C_6H_8O_7$, formerly designated *paramucic acid*, which corresponds with *d*-saccharolactonic acid (p. 717: Ber. **24,** 2141). Reduction changes this lactonic acid into *dl*-galactonic acid (p. 714: Ber. **25,** 1247). The semi-amide of mucic acid on oxidation with hydrogen peroxide in presence of ferric acetate yields the amide of lyxuronic acid, one of the pentose aldehydo-acids (Ber. **54,** 1362). Mucic acid on heating with pyridine to 140° is partly converted into allomucic acid (p. 719), the change being reversible under these conditions.

The ready conversion of mucic acid into heterocyclic derivatives is rather remarkable. Digestion with fuming hydrochloric or hydrobromic acid changes it to furandicarboxylic acid (*dehydromucic acid*):



When mucic acid is heated alone it loses carbon dioxide and becomes converted into furanmonocarboxylic acid (*pyromucic acid*):

$$C_4H_4(OH)_4(CO_2H)_2 = C_4H_3O{\cdot}CO_2H + 3H_2O + CO_2.$$

Heated with barium sulphide it passes in like manner into α-thiophencarboxylic acid (Ber. **18,** 457).

Pyrrole is produced when the diammonium salt is heated:

$$C_6H_8(NH_4)_2O_8 = C_4H_4NH + NH_3 + 2CO_2 + 4H_2O.$$

The action of PCl_5 yields dichloromuconic acid (p. 578).

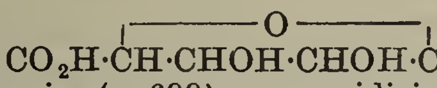
Salts and Esters.—The *di-potassium salt* and *di-ammonium salt* crystallize well and dissolve with difficulty in cold water; the *mono-alkali salts* dissolve readily. The *silver salt*, $C_6H_8Ag_2O_8$, is an insoluble precipitate; *diethyl ester*, m.p. 158°; *tetraacetyl diethyl ester*, m.p. 177° (Ber. **21**, R. 186: C. 1898, II. 963).

(5) **Allomucic acid,** $C_6H_{10}O_8$, m.p. 166–171°, is optically inactive, and more soluble than mucic acid, from which it is obtained on heating with pyridine, by a reversible reaction (Ber. **24**, 2136).

(6) **Talomucic acid,** $CO_2H[CHOH]_4CO_2H$, is known in two space-isomeric modifications:

d-*Talomucic acid*, m.p. about 158° (decomp.), and resulting from the oxidation of *d*-talonic acid (Ber. **24**, 3625).

l-*Talomucic acid*, prepared by oxidizing *β*-rhamnosecarboxylic acid (p. 714) (Ber. **27**, 384).



(7) *iso***Saccharic acid,** $CO_2H\cdot\overset{|\!-\!-\!-\!-\!-\!-\!-\!-\!-\!-\!-\!-\!O\!-\!-\!-\!-\!-\!-\!-\!-\!-\!-\!-\!-\!|}{CH\cdot CHOH\cdot CHOH\cdot CH}CO_2H$, m.p. 185°, $[\alpha]_D = +46{\cdot}1°$, results from glucosamine (p. 699) upon oxidizing it with nitric acid (Ber. **19**, 1258: see also Chitonic and Chitaric acids, p. 714). The acid itself and some of its derivatives are tetrahydrofuran derivatives, as shown by the constitutional formula. Other derivatives are referred to the hydrated form, *i.e.* tetrahydroxyadipic acid, and these are described as nor*iso*saccharic derivatives, *e.g.* ethyl nor*iso*saccharate, $C_6H_8O_8(C_2H_5)_2$, m.p. 73°, which changes in a desiccator to ethyl *iso*saccharate, m.p. 101°. Diacetyl*iso*saccharic ester, m.p. 49° (Ber. **27**, 118).

B. PENTAHYDROXYDICARBOXYLIC ACIDS

Glucopentahydroxypimelic acid, $CO_2H[CHOH]_5CO_2H$, is produced in the oxidation of dextrosecarboxylic acid with nitric acid; *lactone* is crystalline, m.p. 143° (Ber. **19**, 1917).

α-Galapentahydroxypimelic acid, $CO_2H[CHOH]_5CO_2H$, m.p. 171° (decomp.), is formed in the oxidation of *α-d*-galactosecarboxylic acid with nitric acid. It dissolves with difficulty in water, and crystallizes in plates.

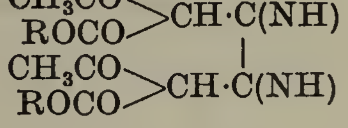
β-Galapentahydroxypimelic acid formed from *β*-galaheptonic acid and nitric acid (Ann. **288**, 155).

9. TETRAKETODICARBOXYLIC ACIDS

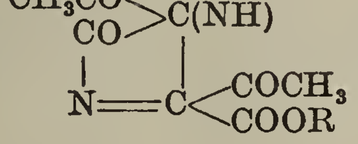
Acetonylacetonedioxalic ester, $C_2H_5O_2C\cdot CO\cdot CH_2COCH_2\cdot CH_2COCH_2\cdot CO\cdot CO_2\text{-}C_2H_5$, m.p. 101°, is prepared from acetonylacetone (p. 405), oxalic ester, and sodium in ethereal solution. Hydrazine produces ethanedipyrazylcarboxylic ester (Ber. **33**, 1220).

αα′-Diacetyl-ββ-diketoadipic acid, $CH_3CO\cdot CH(CO_2H)COCOCH(COCH_3)CO_2H$, is the hypothetical parent substance from which is derived *dicyanobisacetoacetic ester* (1), m.p. 132°. This is prepared from dicyanomonoacetoacetic ester (p. 663), acetoacetic ester, and a little sodium alcoholate. Alkalis convert it first into a yellow *lactam* (2), m.p. 136°, and later into the free *acid*, m.p. 230° (decomp.). Reduction with sodium amalgam, accompanied by simultaneous ketone decomposition, forms *βγ-diamino-αδ-diacetylvaleric ester* (3), m.p. 35° (Ann. **332**, 138):

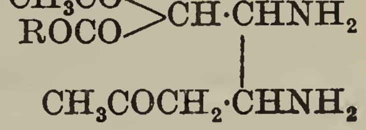
(1)



(2)



(3)



10. TRIKETOTRICARBOXYLIC ACIDS

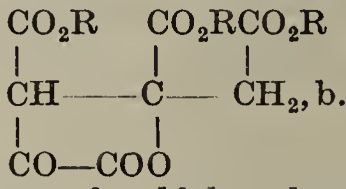
α-Acetyl-ββ′-diketoadipic-α′-carboxylic acid, $CH_3COCH(CO_2H)COCOCH(CO_2H)_2$, has, as a derivative, *dicyanoacetoacetic malonic ester*, $CH_3COCH(CO_2C_2H_5)C(NH)\text{-}C(NH)CH(\cdot CO_2C_2H_5)_2$, m.p. 93°, the reaction product of dicyanoacetoacetic ester (p. 663) and malonic ester (Ann. **332**, 144). But dicyanomalonic ester and sodium acetoacetic ester yield *dicyanomalonicacetoacetic ester lactam*, m.p. 137° (indefinite). Similarly, dicyanocyanoacetic ester and sodium acetoacetic ester give rise to *dicyanocyanoaceticacetoacetic ester lactam*, m.p. 168° (indefinite) (Ann. **332**, 129).

Oxalyldimalonic acid, *ββ′-diketoadipic-αα′-dicarboxylic acid*, $(HO_2C)_2CH\cdot CO\cdot\text{-}$

$COCH(CO_2H)_2$, is the hypothetical parent substance of *dicyanobismalonic acid,* $(HO_2C)_2CHC(NH){\cdot}C(NH){\cdot}CH(CO_2H)_2$, of which the *dilactam* is formed from dicyanogen and sodium malonic ester. Sodium amalgam reduces it to diaminoadipic dicarboxylic acid, which loses CO_2 and becomes changed into ββ′-diaminoadipic acid (p. 660) (Ann. **332**, 122).

11. HYDROXYKETOTETRACARBOXYLIC ACIDS

Oxalocitric lactone ethyl ester,

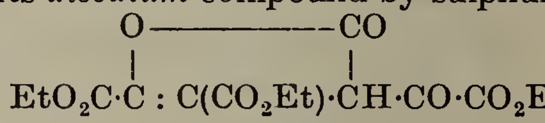


$$\begin{matrix} CO_2R & CO_2R & CO_2R \\ | & | & | \\ CH & —C— & CH_2 \\ | & | & \\ CO & —COO & \end{matrix}$$

b.p. 210°/30 mm., is prepared from two molecules of oxaloacetic ester by aldol condensation and lactone formation (Ann. **295**, 347).

12. DIKETOTETRACARBOXYLIC ACIDS

Dioxalosuccinic ethyl ester, $[EtO{\cdot}CO{\cdot}CO{\cdot}CH(CO_2Et){\cdot}]_2$, is formed by the condensation of succinic and oxalic esters by sodium ethoxide. When distilled under greatly reduced pressure it loses CO and is converted into ethanetetracarboxylic ester. When liberated from its *disodium* compound by sulphuric acid it gives *dioxalosuccinic lactone ethyl ester,*

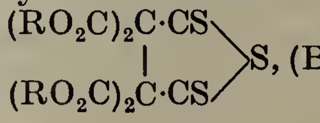


$$EtO_2C{\cdot}\overset{\overset{O\text{————}}{|}}{C} : C(CO_2Et){\cdot}\overset{\overset{\text{————}CO}{|}}{CH}{\cdot}CO{\cdot}CO_2Et$$

m.p. 89° (Ann. **285**, 11).

13. HEXACARBOXYLIC ACIDS

Ethanehexacarboxylic acid, $(COOH)_3C{\cdot}C(COOH)_3$, is known only in the form of its *ethyl ester,* m.p. 101°, which is obtained in small yield by the electrolysis of the sodium salt of methanetricarboxylic ester (*q.v.*) (Ber. **54**, 900). Other derivatives of ethanehexacarboxylic acid are *bis-cyanomalonic ester,* $NC{\cdot}C(CO_2C_2H_5)_2{\cdot}C(CO_2C_2H_5)CN + 1\frac{1}{2}H_2O$, m.p. 57°, which is obtained by electrolysis of sodium cyanomalonic ester (C. 1905, I. 1141). Also, by the action of carbon disulphide and bromine on sodium malonic ester and sodium cyanoacetic ester there is formed dithiotetrahydrothiophentetracarboxylic ester,



$$\begin{matrix} (RO_2C)_2C{\cdot}CS \\ | \\ (RO_2C)_2C{\cdot}CS \end{matrix}\!\!>\!S$$

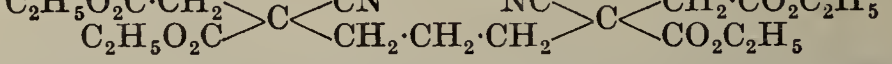
(Ber. **34**, 1043).

Pentane-ααγγεε-hexacarboxylic ester, $(EtO_2C)_2CH{\cdot}CH_2{\cdot}C(CO_2Et)_2CH_2CH(CO_2Et)_2$, m.p. 54°, b.p. 155°/15 mm., is prepared by condensation of two molecules of formaldehyde and three of malonic ester brought about by diethylamine. Its disodium salt with bromine yields a *cyclo*pentane derivative (J.C.S. **77**, 298).

Pentane-αββδδε-hexacarboxylic ester, $CH_2[C(CO_2Et)_2{\cdot}CH_2{\cdot}CO_2Et]_2$, m.p. 64°, b.p. 230–240°/12 mm. (J. pr. Chem. [2] **66**, 112).

Hexane-αγγδδζ-hexacarboxylic ester, $C_2H_5O_2CCH_2CH_2C(CO_2C_2H_5)_2C(CO_2C_2H_5)_2CH_2CH_2{\cdot}CO_2C_2H_5$, is formed from disodium ethanetetracarboxylic ester and two molecules of β-iodopropionic ester. Hydrolysis and decomposition produces diglutaric acid (J.C.S. **85**, 614).

Heptanehexacarboxylic acid. A derivative of this acid is *trimethylenedicyanosuccinic ester:*



$$\begin{matrix} C_2H_5O_2C{\cdot}CH_2 \\ C_2H_5O_2C \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} CN \\ CH_2{\cdot}CH_2{\cdot}CH_2 \end{matrix}\!\!\begin{matrix} NC \\ \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} CH_2{\cdot}CO_2C_2H_5 \\ CO_2C_2H_5 \end{matrix}$$

m.p. 69°, b.p. 215°/7 mm., produced by the interaction of trimethylene bromide on sodium cyanosuccinic ester (C. 1897, II. 520 : 1899, I. 826).

Appendix.—Higher polycarboxylic ethyl esters may be obtained from sodium propane pentacarboxylic ester, chloromalonic ester, and chloropropane pentacarboxylic ester, giving rise to *butaneheptacarboxylic ester,* $C_4H_3(CO_2C_2H_5)_7$, b.p. 280–285°/130 mm., and *hexanedecacarboxylic ester,* $C_6H_4(CO_2C_2H_5)_{10}$, a yellow oil. *Octanetetradecacarboxylic ester,* $C_3H_4(CO_2C_2H_5)_{14}$, is prepared from sodium butaneheptacarboxylic ester and chlorobutaneheptacarboxylic ester. It is the highest-known carboxylic ester, and consists of a thick oil (Ber. **21**, 2111).

CARBOHYDRATES *

This term is applied to a large class of compounds, widely distributed in nature, comprising natural sugars, and substances related to them. They contain six, or a multiple of six, carbon atoms. The ratio of their hydrogen and oxygen atoms is the same as that of these elements in water, hence their name.

Most of the carbohydrates have their origin in plants, although some are probably also produced in the animal organism. Those which occur in the vegetable kingdom meet with the most extensive employment.

Carbohydrates serve for the preparation of alcoholic drinks (p. 142). Sugars, particularly cane sugar, form the basis of many foodstuffs. Starch is the chief ingredient of flour from which bread, the most important food, is made. It is found stored up in potatoes and grain fruits. Cellulose, related to it, is the principal constituent of wood, cotton, etc., and is applied in paper-making and for the production of explosives. The carbohydrates in conjunction with the proteins and fats constitute the most important food-materials for man.

Their molecular complexity is the basis of their arrangement into these classes:

Monosaccharides (Monoses),
Disaccharides,
Trisaccharides,
Polysaccharides.

The monosaccharides, including glucose and fructose, have already been discussed in connection with the hexahydric alcohols, of which they are the first oxidation products (p. 679).

Nearly all of the naturally occurring carbohydrates are optically active. The specific rotatory power is not only influenced by the temperature and concentration of their solutions, but very frequently also by the presence of inactive substances (Ber. **21**, 2588, 2599). Some representatives also exhibit the phenomenon of mutarotation (p. 690). The determination of this rotatory power of the carbohydrates by means of the saccharimeter serves to ascertain their purity, or for the determination of their amount when dissolved: optical sugar test, *saccharimetry*.

Constitution and Classification

Constitutionally, the di- and tri-saccharides are ether-like anhydrides of the monoses. According to the mode of combination of the monoses to form the compounds $C_{12}H_{22}O_{11}$, or, more generally, $nC_6H_{12}O_6 - (n - 1)H_2O$, the following types can be distinguished.

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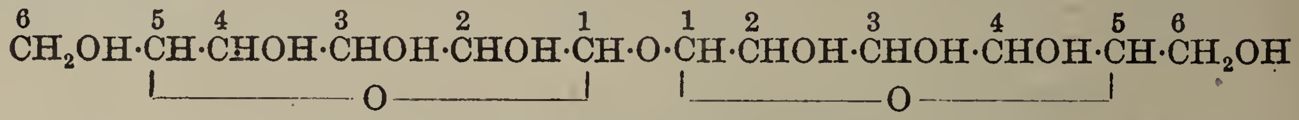
* For literature of carbohydrates, see references given on p. 683.

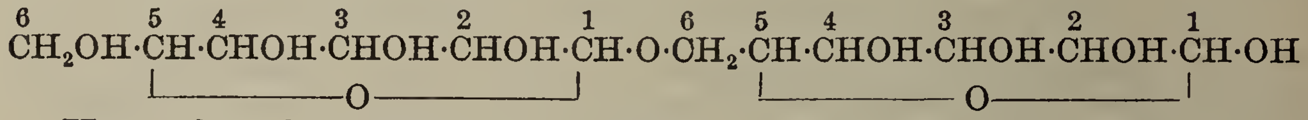
1. *Non-reducing Disaccharides, Trehalose Type.* The monose residues are united by a glucosidic link which involves both reducing groups, *e.g.*:



$$\overset{6}{\mathrm{CH_2OH}}\cdot\underbrace{\overset{5}{\mathrm{CH}}\cdot\overset{4}{\mathrm{CHOH}}\cdot\overset{3}{\mathrm{CHOH}}\cdot\overset{2}{\mathrm{CHOH}}\cdot\overset{1}{\mathrm{CH}}}_{\mathrm{O}}\cdot\mathrm{O}\cdot\underbrace{\overset{1}{\mathrm{CH}}\cdot\overset{2}{\mathrm{CHOH}}\cdot\overset{3}{\mathrm{CHOH}}\cdot\overset{4}{\mathrm{CHOH}}\cdot\overset{5}{\mathrm{CH}}}_{\mathrm{O}}\cdot\overset{6}{\mathrm{CH_2OH}}$$

The characteristic features of this class are their inability to reduce Fehling's solution, and their failure to form osazones. Examples are cane sugar and trehalose.

2. *Reducing Disaccharides. Maltose Type.* Here the glucosidic link involves only one of the reducing groups of the constituent monoses, the other monose residue being attached by one of the 2—6 carbon atoms, *e.g.*:



$$\overset{6}{\mathrm{CH_2OH}}\cdot\underbrace{\overset{5}{\mathrm{CH}}\cdot\overset{4}{\mathrm{CHOH}}\cdot\overset{3}{\mathrm{CHOH}}\cdot\overset{2}{\mathrm{CHOH}}\cdot\overset{1}{\mathrm{CH}}}_{\mathrm{O}}\cdot\mathrm{O}\cdot\overset{6}{\mathrm{CH_2}}\cdot\underbrace{\overset{5}{\mathrm{CH}}\cdot\overset{4}{\mathrm{CHOH}}\cdot\overset{3}{\mathrm{CHOH}}\cdot\overset{2}{\mathrm{CHOH}}\cdot\overset{1}{\mathrm{CH}}}_{\mathrm{O}}\cdot\mathrm{OH}$$

Here the characteristic features are the reduction of Fehling's solution and the formation of osazones. Examples of this class are maltose, cellobiose, lactose, gentiobiose, etc.

Disaccharides of the molecular formula $(C_6H_{10}O_5)_2$ are further anhydrides of the above classes.

Nomenclature.—The disaccharides can be systematically named by employing arabic numerals to indicate the carbon atoms of the monoses involved in the glucosidic link, and figures enclosed in brackets <> to indicate the position of the oxide rings. The disaccharides formulated above, assuming both monose residues to be glucose, can then be described as:

1-Glucosido<1 : 5>-1-glucose<1 : 5> and
1-Glucosido<1 : 5>-6-glucose<1 : 5>.

When this is known, the compounds can be identified as belonging to the α- or β-glucoside series, by the addition of the appropriate Greek letter. The type of sugar residues involved can also be indicated by the furanose-pyranose nomenclature (p. 690).

Determination of Constitution.—The most important information as to the constitution of the di- and poly-saccharides is given by the identification of the constituent monoses. For this purpose, hydrolysis of the polysaccharide by dilute mineral acids or enzymes is employed. The behaviour of a polysaccharide towards Fehling's solution and phenylhydrazine generally permits of a polysaccharide being assigned to one of the classes referred to above.

A more difficult problem is the determination of the position of the links uniting the monose residues. The British school (Haworth, Irvine, Purdie and others) has developed a method of general application, all free hydroxyl groups of the di- and polysaccharide being methylated, and the resulting fully methylated product hydrolysed with 5% hydrochloric acid. Irvine used methyl iodide and silver oxide, Haworth methyl sulphate and alkali as their methylating agents. On hydrolysis of the methylated product, the methyl groups remain attached, and the free hydroxyl groups in the hydrolysed products afford a clue to the position of linkage. The method depends upon the assumption that in the process of methylation, no constitutional alteration such as wandering of methyl groups or change in the position of an oxide ring takes place, and that the constitution of the simple methylhexoses is completely determined: so long as these conditions cannot be completely fulfilled, the solution must be completed by other methods.

The degradation method of Zemplén (Ber. **59**, 1258) for the reducing disaccharides is of great value for this purpose. It consists in treating the readily obtained oximes of the disaccharides with acetic anhydride and sodium acetate, whereby the octaacetylbionic nitriles are formed, the latter being degraded by the action of sodium methylate on a chloroform solution into a disaccharide containing one carbon atom less than the original, NaCN and the acetyl groups being split off in the reaction. (Cellobiose, Ber. **59**, 1254: Lactose, Ber. **60**, 1309: Maltose, Ber. **60**, 1558.)

The position of the oxide rings in the monose residues is determined simultaneously with the determination of the positions in which linkage has taken place: the methods previously referred to are also of value here. Carbohydrates containing a ring other than an amylene oxide one are sometimes characterized by extraordinary ease of hydrolysis and by their capacity to reduce neutral permanganate and to condense very readily with acetone.

The assignation of di- and poly-saccharides to the α- and β-glucoside series has so far been possible only in a limited number of cases.

Synthesis of Disaccharides.—The synthesis of certain disaccharides affords support to the findings obtained above. Fischer, in 1895, by the action of concentrated hydrochloric acid on glucose obtained a disaccharide, which he named *iso*maltose. The synthetic methods starting from the acetobromohexoses are somewhat less equivocal in their results. For instance, from acetobromoglucose in ethereal solution there is obtained by the action of aqueous silver carbonate, together with tetraacetylglucose, the octaacetyl derivative of a disaccharide, which of necessity must belong to the non-reducing series (Ber. **42**, 2776). This demonstrates the limitation of the method.

A more generally applicable method is that of condensing acetobromoglucose with the sodium derivative of a hexose (Fischer, Ber. **35**, 3144). The hexoses so obtained have their constitutions only in part determined.

Pictet has devised a novel synthetic method for disaccharides, equimolecular quantities of two anhydrohexoses being heated together. He succeeded by this method in synthesizing maltose by purely chemical means from glucosan and lævoglucosan (Bull. Soc. Chim. [4], **27**, 652). Further synthetic methods, see Helv. Chim. Acta. **4**, 319, 796: Ber. **54**, 1564. The most important problem in the synthesis of carbohydrates, the introduction of monose residue at a definite position in a second monose molecule, has recently been successfully carried out. The acetone-sugars and partially acylated hexoses and their triphenylmethyl ethers form the starting material. (See Synthesis of gentiobiose, p. 728: Ann. **447**, 27.)

A number of naturally occurring disaccharides can be obtained synthetically by the action of enzymes on their components (see Enzymes).

A. DISACCHARIDES. SACCHAROBIOSES

1. **Pentosidohexoses.**—These yield on hydrolysis one molecule of pentose and one of hexose.

Primverose, 1-*β-xylosido*<1 : 5>-6-*glucose*<1 : 5>, m.p. 209°, $[\alpha]_D$ + 22·7° (initial), — 3·4° (final), occurs as the glucoside *primverin* in various plants, among others in the root of *Primula officinalis. Osazone,* m.p. 220° (Compt. rend. **169**, 871, 975). *Synthesis,* Helferich, Ann. **455**, 168.

A number of hexosidopentoses are obtained by the degradation of hexosidohexoses by Zemplén's method.

1-*α-Glucosido*<1 : 5>-3-*arabinose*<1 : 5> from maltose, obtained as *phenylosazone,* decomp. 195° (Ber. **60**, 1558) : 1-*β-glucosido*<1 : 5>-3-*arabinose*<1 : 5> from cellobiose ; crystalline *acetyl* derivative : *osazone,* decomp. 210° (Ber. **59**, 1254).

1-*Galactosido*<1 : 5>-3-*arabinose*<1 : 5> from lactose, or by the oxidative degradation of calcium lactobionate. $[\alpha]_D$ — 50·3° (initial), — 63° (final, in water). *Benzylphenylhydrazone,* m.p. 214° (decomp.) (Ber. **60**, 1309). 1-*Galactosido*<1 : 5>-2(?)-*arabinose*<1 : 5> from melibiose. Only obtained in solution, and does not form an osazone (Ber. **60**, 923).

2. **Hexosidohexoses.**—These yield on hydrolysis by acids or enzymes two molecules of hexose, according to the equation :

$$C_{12}H_{22}O_{11} + H_2O = 2C_6H_{12}O_6.$$

I. Non-reducing Disaccharides, $C_{12}H_{22}O_{11}$

1. **Glucosidoglucoses.—Trehalose,** 1-*α-glucosido*<1 : 5>-1-*glucose*<1 : 5> is obtained from various plants, especially seaweeds and fungi. The plant *Selaginella lepidophylla* of America is the best source for the preparation of trehalose. Trehalose has m.p. 96–97° and $[\alpha]_D$ + 197°.

*iso***Trehalose,** $[\alpha]_D^{23}$ — 39·4°, is obtained together with tetraacetylglucose from *β*-acetobromoglucose and silver carbonate (Ber. **42**, 2776). *Octaacetyl derivative,* m.p. 178° $[\alpha]_D^{20}$ — 17·2° (in benzene).

2. **Glucosidofructoses.—Saccharose,** *cane sugar,* $C_{12}H_{22}O_{11}$, the most important of the sugars, occurs in the juice of many plants, chiefly in sugar cane (*Saccharum officinarum*) (20 per cent. of the juice), in some varieties of maple, in the sorghum (*Sorghum saccharatum*), and in beet-roots (*Beta maritima*) (10–20 per cent.), from which it is prepared on a commercial scale ; and also in the seeds of some plants (Ber. **27**, 62).

Whilst the hexoses occur mainly in fruits, sucrose is usually contained in the stalks of plants. The sugar cane contains, together with the sucrose, lævulose and dextrose, of which the quantity diminishes with the growth of the plant.

Historical.—Sugar has been obtained from sugar cane from the earliest times. In the Middle Ages sugar cane was a rarity in Germany ; it was only after the discovery of America that it was gradually introduced as a sweetening agent. In 1747 Marggraf, in Berlin, discovered sucrose in beet-roots, an observation which became the basis of the beet-sugar industry. In 1801 Achard, in Silesia, erected the first beet-sugar factory. The continental blockade forced by Napoleon I hastened the development of the new industry, which during the last fifty years has attained a constantly increasing importance in Germany. The total sugar production of the world in 1930–1 was some 29 million tons, about 18 millions being derived from sugar cane and 11½ million tons from beet.

*Technical Production.** The sugar is removed from the cane or from the

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* *Claassen* : Die Zuckerfabrikation, 4. Aufl. 1918, (Magdeburg, Schallehn und Wollbrück) : *Herzog,* Chemische Technologie der Organischen Verbindungen, 2. Aufl. 1927, (Heidelberg, Winter). Report on the Sugar Beet Industry, H.M. Stationery Office, London, 1931.

finely divided beets by the diffusion process. The saccharine juice diffuses through the cell walls, whereas the colloids in the latter remain behind. The filtered sap is heated to 80–90° with milk of lime, to saturate the acids, and precipitate the proteins. The juice is next treated with carbon dioxide, phosphoric acid, or SO_2 (to arrest fermentation), filtered through animal charcoal, and is concentrated in vacuum pans till it crystallizes. The mother-liquor, *molasses,* is separated by centrifugation, and the solid is washed with a pure sugar solution ("*Klärsel*") or purified by recrystallization, and thus forms refined sugar.

Sugar may be obtained from the syrupy mother liquor—the molasses, which cannot be brought to crystallization—by *osmosis,* depending upon diffusion through parchment paper, in apparatus similar to filter presses or by elution (Scheibler, 1865). The sparingly soluble saccharates of lime and strontium are obtained from the molasses (see below) and these are freed from impurities by washing with water or dilute alcohol. The purified saccharates are afterwards decomposed by carbon dioxide, and the juice which is thus obtained is further worked up.

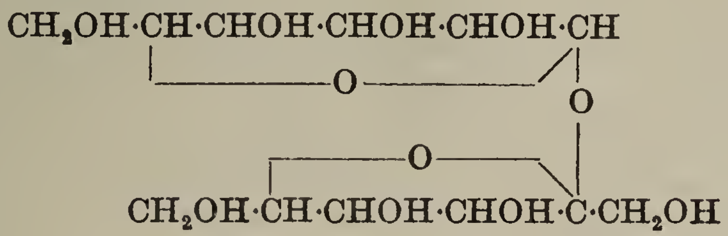
The molasses is also converted into *rum* (p. 142).

Properties.—When its solutions are evaporated slowly, sucrose separates in large monoclinic prisms, and dissolves in one-third part water of medium temperature ; it dissolves with difficulty in alcohol. It has $[\alpha]^{20}_{D} + 66{\cdot}5°$. It melts at 160°, and on cooling forms a glassy mass (barley sugar) which very slowly becomes crystalline and loses its transparency. At 190–200° it changes to a brown non-crystallizable mass, called *caramel,* which finds application in colouring foodstuffs.

The quantity of sugar in solution may be determined by polarization, using the apparatus of *Soleil-Ventzke-Scheibler,* or the half-shadow instrument devised by *Schmidt and Hänsch* (Ber. **27,** 2282), as well as from the specific gravity by means of the saccharimeter of *Brix.*

Reactions and Constitution.—By the action of enzymes, or by heating with dilute acids, cane sugar is converted into a mixture of equimolecular amounts of *d*-glucose and *d*-fructose. The direction of the optical activity is reversed in this reaction, and the product is described as *invert sugar.* Cane sugar does not reduce Fehling's solution, but after this inversion, its products do so. Concentrated sulphuric acid converts it into a black, humus-like substance. When heated with nitric acid, saccharose is oxidized to *d*-saccharic acid, tartaric acid and oxalic acid. When heated to 160° with acetic anhydride, the *octaacetyl derivative,* $C_{12}H_{14}O_3(OAc)_8$, m.p. 67°, is produced (Ber. **34,** 4347).

The constitution of saccharose is established by the formation of 2 : 3 : 4 : 6-tetramethylglucopyranose and 1 : 3 : 4 : 6-tetramethylfructofuranose when the octamethyl derivative of saccharose is hydrolysed (J.C.S. 1916, **109,** 1314 : **1927,** 2308, 2432). It is therefore to be represented as a 1-glucosido<1 : 5>-2-fructose<2 : 5>. Whether the sugar residues are linked as α- or *β*-glucosides cannot at present be stated with certainty.



The above formula is supported by the synthesis of the compound by the action of phosphorus pentoxide on a chloroform solution of equimolecular quantities of 2 : 3 : 4 : 6-tetraacetylglucose and 1 : 3 : 4 : 6-tetraacetylfructose (furanose derivative) followed by hydrolysis of the octaacetylsaccharose so obtained (Pictet, Compt. rend. **186**, 724).

Octamethylsucrose forms a syrup, b.p. 176°/0·05° mm., $[\alpha]_D$ + 66·7° (methyl alcohol) (J.C.S. **109**, 1314 : **123**, 301).

Saccharates.—Sucrose unites with bases to form saccharates. $C_{12}H_{22}O_{11}{\cdot}CaO + 2H_2O$ is precipitated by alcohol, whilst $C_{12}H_{22}O_{11}{\cdot}2CaO$ crystallizes on cooling. $C_{12}H_{22}O_{11}{\cdot}3CaO$ dissolves with great difficulty (Ber. **16**, 2764). Similar compounds are formed with the oxides of strontium and barium (see above) (Ber. **16**, 984).

Thiotrehaloses.—*Octaacetylthio*iso*trehalose* is obtained as colourless needles, m.p. 174°, $[\alpha]_D$ − 38·2°, by the action of potassium sulphide on acetobromoglucose. It can be saponified to *thio*iso*trehalose*, m.p. 174°, $[\alpha]_D$ − 84·7°, and only by prolonged heating with acids is it hydrolysed with loss of H_2S (Ber. **50**, 793).

Selenotrehaloses, see Ber. **50**, 800.

II. Reducing Disaccharides $C_{12}H_{22}O_{11}$

Maltose, *malt sugar, maltobiose,* $C_{12}H_{22}O_{11} + H_2O$, $[\alpha]^{20}_D$ + 137° (equilibrium value), is a sugar formed, together with dextrin, by the action of malt diastase on starch, as in the mash of whisky and beer. It is also an intermediate product in the action of dilute sulphuric acid on starch, and of the ferment *diastase* on glycogen (p. 733). It is prepared from starch paste by means of diastase (Ann. **220**, 209). It is capable of direct fermentation (Willstätter, Z. physiol. Chem. **152**, 202).

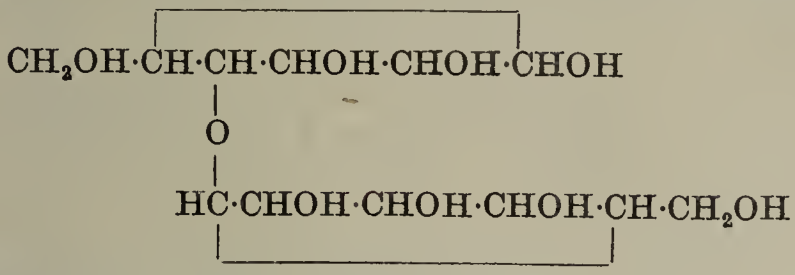
Maltose is readily fermented by yeast. Under ordinary conditions the maltose is hydrolysed by the enzyme maltase into two molecules of glucose, which then undergo fermentation. In an acid medium, p_H 4·5, however, where maltase no longer acts, maltose can be directly fermented (Z. physiol. Chem. **152**, 202). Maltose reduces Fehling's solution, about two-thirds as much as an equal quantity of glucose.

Maltose is not further attacked by diastase. By heating with dilute acids it is converted into glucose, with the addition of the elements of water. Nitric acid oxidizes maltose to *d*-saccharic acid (p. 717) and chlorine water to maltobionic acid, $C_{12}H_{20}O_{11}$, which can be hydrolysed to glucose and *d*-gluconic acid. By the addition of hydrocyanic acid, it can be converted into maltosecarboxylic acid, $C_{12}H_{23}O_{11}{\cdot}COOH$; which can be hydrolysed to glucose and glucosecarboxylic acid (Ann. **272**, 200). When heated with lime water, maltose yields " *iso*saccharin " (p. 676).

Octaacetylmaltose, $C_{12}H_{14}O_3(OAc)_8$, m.p. 156°, $[\alpha]_D$ + 123°, yields with liquid hydrogen chloride *heptaacetylchloromaltose,* $C_{12}H_{14}O_3(OAc)_7Cl$, two forms of which, m.p. 67° (Ber. **35**, 840) and m.p. 118° (Ann. **377**, 186), probably represent the α- and β-forms of the compound. A *third* form, m.p. 112–114° (Ber. **55**, 922), is possibly derived from a γ-form of the sugar. *Heptaacetylmaltose nitrate,* $C_{12}H_{14}O_3(OAc)_7O{\cdot}NO_2$, m.p. 94°, is obtained by the action of fuming nitric acid on the octaacetyl compound in chloroform solution. The two latter compounds yield with methyl alcohol, *heptaacetylmethylmaltoside,* m.p. 128°, which yields on removal of the acetyl groups, *β-methylmaltoside,* m.p. 94° (Ber. **34**, 4343 : **35**, 840). *Heptamethylmethylmaltoside,* b.p. 190°/0·09 mm., $[\alpha]_D$ + 81·4° (in water).

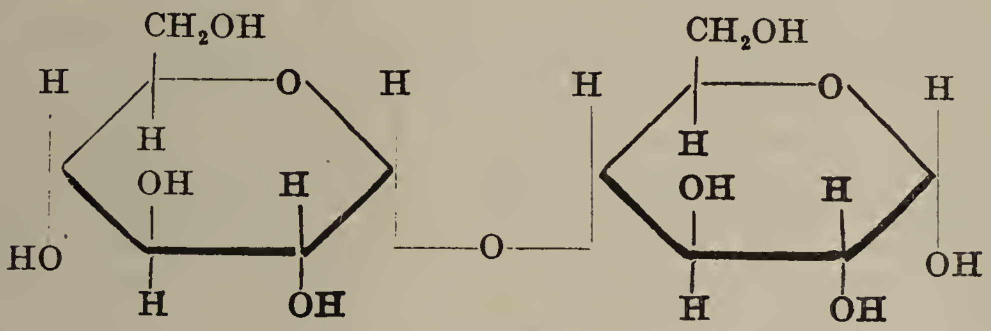
Maltosazone, m.p. 206°, is decomposed by benzaldehyde yielding maltosone (Ber. **20**, 831 : **35**, 3142).

Constitution of Maltose.—Heptamethylmethylmaltoside is hydrolysed by 5% hydrochloric acid to equimolecular amounts of 2 : 3 : 4 : 6-tetramethylglucose and 2 : 3 : 6-trimethylglucose, both compounds being derivatives of glucopyranose. This shows that the second molecule of glucose is attached at the 4th carbon atom (J.C.S. **1926**, 862). This constitution is confirmed by the degradation products of maltoseoxime (Ber. **60**, 1555). The disaccharide cellobiose (see below) is found to have the same structure as maltose, and as maltose is hydrolysed by maltase which is specific for α-glucosides, whereas cellobiose is hydrolysed by emulsin, which attacks β-glucosides, these compounds can be represented as the α- and β-glucosidic forms of the compound

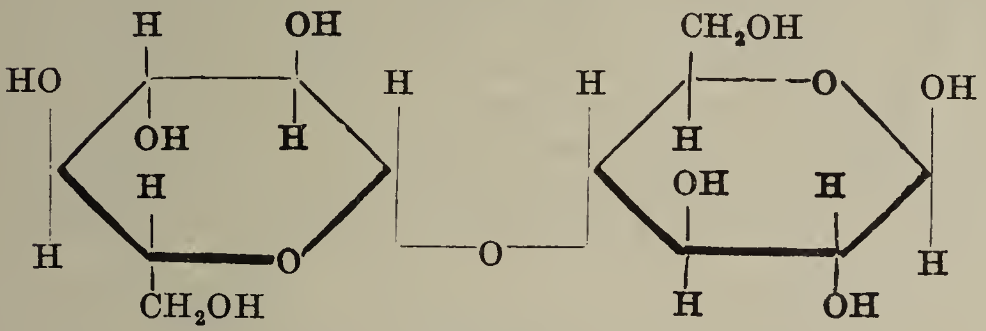


$$\begin{array}{l} CH_2OH{\cdot}CH{\cdot}CH{\cdot}CHOH{\cdot}CHOH{\cdot}CHOH \\ \qquad\quad | \\ \qquad\quad O \\ \qquad\quad | \\ \qquad\quad HC{\cdot}CHOH{\cdot}CHOH{\cdot}CHOH{\cdot}CH{\cdot}CH_2OH \end{array}$$

and represented by the following stereochemical formulæ :



Maltose.

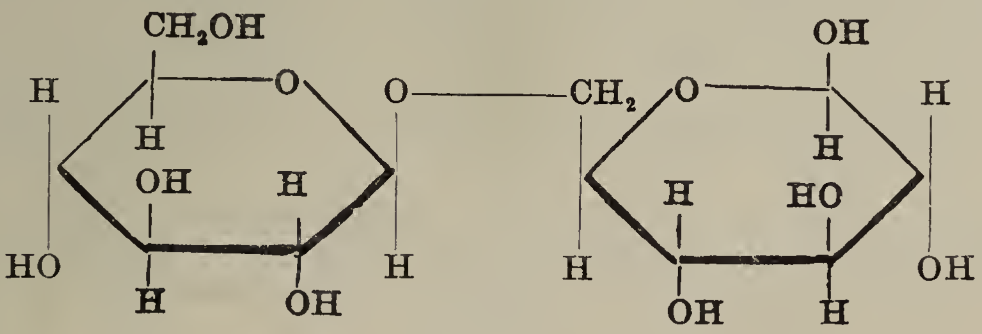


Cellobiose.

Synthesis of Maltose.—(1) Biochemically, by the reversible action of yeast maltase on *d*-glucose (Ber. **57**, 1576).

(2) By purely chemical methods : (*a*) By partial hydrolysis of the dextrin obtained from equimolecular quantities of glucosan and lævoglucosan (Bull. Soc. Chim. [4], **27**, 652). (*b*) By heating equimolecular amounts of α- and β-glucose to 160°. Maltose was identified as the octaacetate, phenylosazone and octanitrate (Pictet, Compt. rend. **184**, 1512).

Gentiobiose (below) is a 1-β-glucosido-6-glucose, and has the configuration :



Gentiobiose.

Cellobiose (formula, see above) decomposes at 225° and has $[\alpha]_D + 33{\cdot}7°$ (final value). It is obtained by hydrolysis of *octaacetylcellobiose*, m.p. 228° (Ber. **12**, 1941 : Helv. Chim. Acta. **4**, 174 : Ber. **54**, 767 : **59**, 1258). It is not fermented by yeast, but is hydrolysed by emulsin. Its constitution is based upon the degradation of its oxime (Ber. **59**, 1254) and on the products of hydrolysis of the methyl ester of octamethylcellobionic acid (J.C.S. **1927**, 2809).

Acetobromocellobiose, m.p. 180° (decomp.), $[\alpha]_D + 95°$ (Ber. **43**, 2536). *Acetochlorocellobiose :* Monatsh. **22**, 1033.

Heptaacetylcellobiose, m.p. 195°, $[\alpha]_D + 20°$, is obtained from acetobromocellobiose and silver carbonate (Ber. **43**, 2536).

Cellobial, m.p. 134–135°, $[\alpha]_D - 19{\cdot}8°$, is obtained by reduction of acetobromocellobiose with zinc dust and acetic acid and hydrolysis of the hexaacetyl compound with methyl alcoholic ammonia (Ber. **47**, 2057). *Thio derivatives* of cellobiose, see Z. physiol. Chem. **172**, 169.

*iso***Maltose** (1), $C_{12}H_{22}O_{11}$, $\frac{1}{2}H_2O$, decomp. about 170°, $[\alpha]_D + 100°$ to 97° (final), is obtained from *d*-glucose by the action of concentrated hydrochloric acid, together with a little gentiobiose (Ber. **23**, 3687 : **28**, 3024 : Helv. Chim. Acta. **9**, 614 : *cf.* Ber. **59**, 1983), or by hydrolysis of dilævoglucosan with concentrated hydrochloric acid (Helv. Chim. Acta. **5**, 876 : **9**, 621). *β-Octaacetyl derivative*, amorphous, m.p. 72–77°, $[\alpha]_D + 93{\cdot}7°$. *α-Octaacetyl derivative*, $[\alpha]_D + 115°$, from the *β*- compound by heating with acetic anhydride and zinc chloride. *Osazone*, m.p. 167°.

(2) Obtained by Lintner from starch amylopectin (*q.v.*), $[\alpha]_D + 140°$. *Osazone*, m.p. 152° (Z. angew. Chem. **5**, 268 : *cf.* J.C.S. **123**, 2666).

Gentiobiose (constitution, see above), m.p. 191°, $[\alpha]_D + 9{\cdot}6°$ (equilibrium), is obtained by partial hydrolysis of gentianose. *Osazone*, m.p. 164°, $[\alpha]_D + 10{\cdot}7°$. *Octaacetyl derivative*, m.p. 190°. Synthesis : (1) Biochemical, by the prolonged action of emulsin on a 5% glucose solution (Compt. rend. **157**, 732). (2) Chemical, Helferich, Ann. **447**, 28 (constitution, J.C.S. 1923, **123**, 3120). Gentiobiose is the sugar of the glucoside amygdalin. Synthesis of amygdalin from heptaacetylbromogentiobiose, see Ber. **57**, 1767.

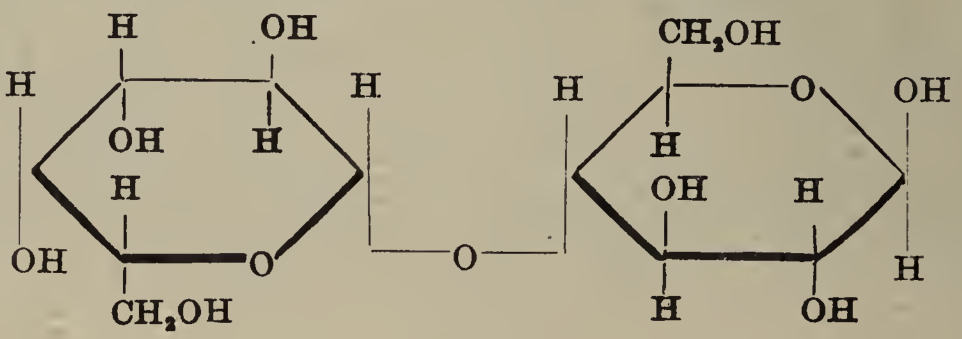
Cello*iso*biose is formed as a by-product in the acetolytic breakdown of cellulose (Z. angew. Chem. **33**, 100). It has m.p. 195°, $[\alpha]_D + 24{\cdot}6°$ (equilibrium value in water). *Osazone*, m.p. 165°. The existence of cello*iso*biose is denied by Haworth, Hirst and Ant-Wuorinen, J.C.S. **1932**, 2368.

2. **Glucosidomannoses.**—A 1-*β-glucosido*<1 : 5>-4-*mannose* is obtained by the action of perbenzoic acid on cellobial. It has m.p. 176° (anhydrous) and $[\alpha]_D + 10{\cdot}7°$ (equilibrium) and gives the same *osazone*, m.p. 198°, as cellobiose. Hydrochloric acid or emulsin hydrolyse it to *d*-glucose and *d*-mannose. *Octaacetyl derivative*, m.p. 196°, $[\alpha]_D + 33{\cdot}2°$ (Ber. **54**, 1564).

3. **Glucosidogalactose.**—A glucosidogalactose of uncertain constitution has been obtained from acetochloroglucose and sodium galactose (Ber. **58**, 1184 : **59**, 2101). *Osazone*, m.p. 174° (Ber. **35**, 3148).

4. **Glucosidofructoses.**—**Turanose**, 1-*glucosido*<1 : 5>-6-*fructose*<2 : 5>, $[\alpha]_D + 65°$, is the sole representative of this class and is obtained by partial hydrolysis of the trisaccharide melezitose (*q.v.*) (Ber. **59**, 1655, 2539 : J.C.S. **1927**, 588).

5. **Galactosidoglucoses.**—**Lactose**, *milk sugar*, is the most important representative of this class, and has the constitution of 1-*β*-galactosido<1 : 5>-4-glucose<1 : 5> (Ber. **59**, 2402 : J.C.S. **1927**, 544). Its configuration is represented as follows :



Lactose has not been isolated from any vegetable source, but occurs in large quantities in the milk of mammals (human milk contains some 6–7%, cow's milk about 4%) and sometimes in the urine during pregnancy and the puerperium. It was discovered in 1615 by Fabriccio Bartoletti of Bologna.

It is obtained from whey by evaporation, the sugar which separates being purified by recrystallization.

It has been synthesized by Pictet by heating together equimolecular amounts of β-glucose and β-galactose (Compt. rend. **185**, 332 : Helv. Chim. Acta. **11**, 209).

Lactose forms rhombic prisms of the composition, $C_{12}H_{22}O_{11} + H_2O$, which lose their water of crystallization at 140° and melt with decomposition at 205°. It is soluble in 6 parts of cold and 2·5 of hot water, but is insoluble in alcohol. It has a faintly sweet taste. The aqueous solution is dextrorotatory, and exhibits mutarotation. The ordinary lactose of commerce is the α-form and has $[\alpha]_D + 90°$. The β-form has $[\alpha]_D + 35°$ and the equilibrium mixture + 55°.

Reactions.—Lactose resembles the hexose in reducing an ammoniacal silver solution in the cold, and an alkaline copper solution (Fehling's solution) on heating.

Lactose is decomposed into galactose and *d*-dextrose by being heated with dilute acids. It is only slowly attacked by yeast, but it readily undergoes lactic acid fermentation (p. 688). Nitric acid converts it into *d*-saccharic and mucic acids. Bromine produces *lactobionic acid*, $C_{12}H_{22}O_{12}$, which splits up into *d*-gluconic acid and *d*-galactose ; whilst oxidation with H_2O_2 breaks it down, as it does the aldoses (p. 673) into galacto-arabinose, $C_{11}H_{20}O_{10}$ (*cf.* Ber. **59**, 2408). The latter forms an *osazone*, m.p. 237°, and is hydrolysed into *d*-galactose and *d*-arabinose (Ber. **33**, 1802). Lactose takes up hydrocyanic acid and forms ultimately *lactosecarboxylic acid*, $C_{12}H_{23}O_{11}\cdot CO_2H$, which decomposes into *d*-glucoheptonic acid (p. 715) and *d*-galactose (Ann. **272**, 198). See also *iso*Saccharin (p. 676).

Lactosazone, $C_{12}H_{20}O_9(N_2HC_6H_5)_2$, m.p. 200° (Ber. **20**, 829). *Octoacetyllactose*, $C_{12}H_{14}O_3[OCOCH_3]_8$, m.p. 106°, yields, with fluid HCl, *heptaacetylchlorolactose*, $C_{12}H_{14}O_3(OCOCH_3)_7Cl$. *Heptaacetylbromolactose* is formed from lactose and acetyl bromide. The two last-named lactose compounds exhibit polymorphism. When treated with methyl alcohol and silver carbonate, they yield *heptaacetylmethyllactoside*, $C_{12}H_{14}O_3(OCOCH_3)_7CH_3$ (Ber. **35**, 841 : C. 1902, II. 1416).

Lactic acid forms a crystalline compound with *aminoguanidine nitrate* (Ber. **28**, 2614).

α-*Galactosan* (Helv. Chim. Acta. **5**, 444).

Melibiose, 1-α(?)-*galactosido*<1 : 5>-6-*glucose*<1 : 5> (Haworth, J.C.S. **1927**, 1527, 3146), m.p. 85° (indefinite), $[\alpha]_D + 143°$, is obtained from raffinose by fermentation with top yeasts or by mild acid hydrolysis (C. 1902, I. 524). It occurs naturally in wild mallow (Ber. **53**, 2076). It is hydrolysed by emulsin. *Octaacetyl derivative*, m.p. 170°, $[\alpha]_D + 98{\cdot}1°$ (C. 1904, I. 1643). Melibiose has been synthesized from diglucosan and di-α-galactosan (Helv. Chim. Acta. **9**, 806 : **10**, 280). The synthetic product yields a *hydrazone*, m.p. 142°, and *osazone*, m.p. 144°, and an *octaacetate*, m.p. 175°.

6. **Galactosidogalactoses.**—Two disaccharides of uncertain constitution have been obtained from *d*-galactose by the synthetic action of emulsin. **A**, $[\alpha]_D + 35°$. B, $[\alpha]_D + 53°$. *Osazone*, m.p. 194° (Compt. rend. **164**, 443, 521).

B. TRISACCHARIDES $C_{18}H_{32}O_{16}$

I. **Non-reducing Trisaccharides.**—The tri- and tetra-saccharides which occur in various plants are attacked by enzymes which occur in the intestinal canal of invertebrates. The higher animals possess no enzymes capable of dealing with them and yeasts only attack them slowly.

Gentianose, 1-*β-glucosido*<1 : 5>-6-*α-glucosido*<1 : 5>-2-*fructose*<2 : 5> (J.C.S. **123**, 3120), occurs together with cane sugar in gentian roots. It has m.p. 209° and $[\alpha]_D + 33°$. It is hydrolysed by emulsin into *d*-glucose and cane sugar and by yeast saccharase into gentiobiose and fructose.

Melezitose, *melecitose,* $C_{18}H_{32}O_{16} + 2H_2O$, is 1-*glucosido*<1 : 5>-6-*fructosido*<2 : 5>-1-*glucose* (Ber. **59**, 1655, 2539 : J.C.S. **1927**, 588). It occurs in various mannas, that occurring on the Douglas Fir being a good source for its preparation (J.A.C.S. **40**, 1456), m.p. 148°, $[\alpha]_D + 88{\cdot}5°$. It is hydrolysed by dilute acids to turanose and glucose, but is not attacked by yeast.

Raffinose, *melitose, melitriose,* $C_{18}H_{32}O_{16} + 5H_2O$, is 1-*galactosido*<1 : 5>-6-*α-glucosido*<1 : 5>-2-*fructose*<2 : 5> (J.C.S. 1923, **123**, 3125 : **1927**, 1527). It has m.p. 122° and $[\alpha]_D + 104°$. It occurs in large amount in Australian manna from *Eucalyptus,* in cotton-seed meal, and in small amount in sugar-beets. It is more soluble than sucrose and accumulates in the molasses in sugar manufacture. From the molasses it is obtained together with the sucrose (Ann. **232**, 173). On account of the high rotatory power of its pointed crystals, it is referred to as "*plus sugar.*" Estimation, see Ber. **19**, 2872, 3116. Raffinose is hydrolysed by emulsin into galactose and sucrose and by invertase into fructose and melibiose.

II. **Reducing Trisaccharides. β-Glucosidomaltose,** m.p. 202°, $[\alpha]_D + 165°$, is obtained by the action of malt diastase on β-hexaamylose at 70° : yeast maltase decomposes it into *d*-glucose and *iso*maltose, emulsin into glucose and maltose. *Phenylosazone,* m.p. 122° (Ling and Nanji, J.C.S. **123**, 2678).

Mannotriose, m.p. 150°, $[\alpha]_D + 167°$, is obtained by the action of yeast on stachyose (see below). *Osazone,* m.p. 122–124°. It is hydrolysed by acids to 2 molecules of galactose and one of glucose. Its constitution is probably a digalactosidoglucose (Biochem. Z. **44**, 446 : Bull. Soc. Chim. [3] **27**, 947).

Rhamninose, m.p. 135–140°, $[\alpha]_D - 41°$, occurs as a glucoside in the Persian berry (*Rhamnus infectoria*). On hydrolysis by acids it is hydrolysed into 1 mol. of galactose and 2 of rhamnose (Compt. rend. **129**, 725 : Rec. Trav. Chim. **42**, 380).

Some trisaccharides of this type have been synthesized, *e.g.* cellobiosidoglucose, lactosidoglucose (Ann. **450**, 229).

C. TETRASACCHARIDES

Stachyose, $C_{24}H_{42}O_{22}$, m.p. 167–170, $[\alpha]_D + 148°$, is a non-reducing tetrasaccharide which occurs in the tubers of *Stachys tubifera,* in ash manna and in other plants. It is hydrolysed by acids into fructose (1 mol.), glucose (1 mol.), and galactose (2 mols.) (*cf.* Ber. **43**, 2230).

D. SUGAR ANHYDRIDES $(C_6H_{11}O_5)_{2 \text{ or } 3}$

A number of di- and trisaccharides are derived from hexoses according to the scheme :

$$nC_6H_{12}O_6 - nH_2O = (C_6H_{11}O_5)_n$$

These can be regarded as derived from the above di- and trisaccharides by loss of a further molecule of water. Their constitution is undetermined. Among them may be included (1) the *polyamyloses* prepared by Schardinger from starch by the action of the *Bacillus macerans.* Pancreatic amylase partially converts it to maltose (Karrer) (Ber. **45**, 2533 : **46**, 2959 : **54**, 1281 : **55**, 153, 1433 : Helv. Chim. Acta. **4**, 169, 263).

(2) **Dihexosan,** $C_6H_{10}O_5)_2$, $[\alpha]_D + 155°$ (water) (*Acetate,* $[\alpha]_D + 142°$), and **trihexosan,** $C_6H_{10}O_5)_3$, $[\alpha]_D + 166°$, are obtained by the depolymerization of starch or amylopectin by heating with glycerol at 200°.

A glucosido-anhydromannose (Ber. **54**, 1564) and glucosido-anhydroglucose (Helv. Chim. Acta. **4**, 319) have been prepared.

E. POLYSACCHARIDES

The polysaccharides with the general formula $(C_6H_{11}O_5)_n$, where n is a large number, differ much more from the monosaccharides than do the di- and trisaccharides already described. The polysaccharides were until recently regarded as amorphous, but X-ray examination (Ber. **53**, 2162 : **54**, 1283) has shown that starch, inulin and cellulose possess a crystalline structure : glycogen alone appears to be really amorphous. The polysaccharides are converted by the action of acids or of enzymes, through the intermediate stages of the comparatively little investigated dextrins finally into monoses. The alcoholic nature of the polysaccharides is demonstrated by their ability to form acetyl compounds, nitric esters and methyl ethers. The polysaccharides can be divided into starches, gums and cellulose.

There are certain gums, like cherry gum and wood gum (p. 736), which yield pentoses by hydrolysis. They are, therefore, called *pentosans* to distinguish them from the *hexosans*—the polysaccharides, which break down into hexoses when they are hydrolysed (Ber. **27**, 2722).

On experiments for determining the molecular magnitude of the polysaccharides such as starch, glycogen, cellulose, by chemical and physical means, see C. 1906, I. 655, etc.: methylated starch, Helv. Chim. Acta. **4**, 185.

Starches

1. **Starch,** *amylum*, $(C_6H_{10}O_5)_n$, is the most important assimilation product of the plant cell. Baeyer suggested that the mechanism of this was the hydrogenation of carbon dioxide to formaldehyde, and the subsequent condensation of this to starch : plants are also capable of forming starch from certain carbohydrates such as glucose, fructose, galactose or maltose or cane sugar. Starch is the typical reserve material of plants and is laid down in granules which vary in size in different plants. According to X-ray investigations, starch crystallizes in the rhombohedral system (Ber. **53**, 2165).

Recent investigations have confirmed the suggestion of Nägeli (1858) and Maquenne (1904) that native starch really consists of two components—*amylose*, the internal portion of the granules, and *amylopectin*, the outer portion. Amylose is free from electrolytes, but amylopectin contains about 0·175% P, probably in the form of a phosphoric ester. Electrolyte-free amylopectin is described as erythroamylose. (Separation of starch into its components, see Ber. **57**, 888 : J.C.S. **123**, 2672.) The amylopectin is responsible for the ability of starch to form a gel.

The blue coloration produced by iodine is characteristic of starch, both the soluble variety and that contained in the granules (Ber. **25**, 1237 : **27**, R. 602 : **28**, 385, 783 : C. 1897, I. 408, 804 : 1902, II. 26). Heat discharges the coloration, but it reappears on cooling. The coloration with iodine is due to an adsorption phenomenon, and the presence of iodine ions facilitates its development. Amylose is coloured a pure blue, and amylopectin violet-brown. As native starch is coloured a pure blue with iodine, presumably the amylose first takes up the iodine, and the amylopectin later.

The property of pectization is of the greatest importance. Starch is insoluble in cold water, but on heating swells up, and at a definite temperature becomes a viscous paste. This temperature is a characteristic for different starches. (Rice-starch, 72°, Maize- 67°, Rye- 56°, Wheat- 62°, Potato- 72°.) This property is due to the amylopectin. Pure amylose does not form a paste.

Quantitative Estimation.—(1) Colorimetric with iodine (Ber. **28**, R. 1025). (2) Hydrolysis of the starch to glucose, and estimation of the latter either polarimetrically or by reduction methods.

Degradation of Starch. (1) *Soluble Starch.*—By partial depolymerization of starch a product can be obtained which is soluble in water. It still gives a blue colour with iodine and has no reducing properties. Soluble starch is not a definite compound, but a mixture of depolymerized products, still very closely allied to starch. The principal methods for its preparation are Lintner's, where the starch is treated with 7% HCl for 7 days at room temperature and Zulkowsky's, where the starch is heated in glycerol to 190°.

(2) *Distillation of Starch.*—By dry distillation in vacuo lævoglucosan is produced (Compt. rend. **166**, 38: p. 696): at ordinary pressures, maltol and *iso*maltol.

(3) Heating with *dilute acids* converts starch into dextrin and eventually into glucose (Kirchhoff, 1811).

(4) *Enzymatic Breakdown.*—(*a*) By means of *amylases.* The enzymes which attack starch are collectively referred to as amylases or diastases. They occur in both the animal and vegetable kingdoms, wherever it is necessary for starch to be brought into solution. Particularly rich sources of amylase are malting barley (malt diastase), saliva and pancreatic juice. The final products of diastase action are disaccharides, and malt diastase yields about 80% of maltose (O'Sullivan, J.C.S. 1872, **25**, 879) and 20% of *iso*maltose (Lintner, Z. angew. Chem. 1892, **5**, 268), the latter being produced from the amylopectin (Ling and Nanji, J.C.S. **123**, 2677). The reaction involves the intermediate formation of imperfectly characterized dextrins. Amylopectin is broken down by precipitated malt diastase to a hexatriose, probably β-glucosidomaltose (see p. 730) which is further broken down by yeast maltase to glucose and *iso*maltose (Ling and Nanji, *loc. cit.*).

It should be noted that in general the hydrolysis of natural starch by diastases comes to an end when about 65% of maltose has been produced. This inhibition can be overcome by the addition of a coenzyme which exists in yeast, and by this means starch can be converted quantitatively into disaccharides (Ber. **56**, 1762: Biochem. Z. **142**, 108: **148**, 336).

(*b*) *Bacillus macerans* (Schardinger, Zentr. Bakt. 1908, [ii] **22**, 98) converts starch to so-called " crystalline dextrins," which are more recently referred to as polyamyloses. These polyamyloses occupy a special position among the breakdown products of starch, in that they are not converted into maltose by malt diastase.

(5) *Acetolysis.*—Karrer succeeded in 1921 (Helv. Chim. Acta. **4**, 263) in obtaining acetobromomaltose quantitatively by the action of acetyl bromide on starch.

(6) *Heating with Glycerol.*—By heating starch with glycerol at 200°, Pictet (Helv. Chim. Acta. **5**, 640) obtained di- and tri-hexosans (p. 730).

(7) *Methylation of Starch.*—The methylation of starch to a trimethyl-derivative was carried out satisfactorily by Haworth, Hirst and Webb in 1928 (J.C.S. **1928**, 2681), by acetylating starch and then simultaneously methylating and de-acetylating the product by the use of dimethyl sulphate and alkali in acetone solution. The yield of trimethyl starch, which gives 2 : 3 : 6-trimethyglucose on hydrolysis, was 89%. Irvine and MacDonald (J.C.S. **1926**, 1502) obtained the same compound with greater difficulty by direct methylation. The introduction of two methyl groups per glucose residue can be fairly readily carried out (Karrer, Helv. Chim. Acta. **4**, 185).

Constitution of Starch.—In spite of the large amount of work which has been done, the constitution of starch must still be regarded as an unsolved problem. Purely chemical methods are possibly too energetic for the elucidation of its constitution: they do not preclude the possibility of unexpected changes taking place in the molecule of native starch. The purely chemical findings are on this account sometimes contradictory (*cf.* Helv. Chim. Acta. **5**, 195, and

J.C.S. **123**, 898). It should be noted, however, that the various degradation methods when applied to amylose always yield products containing two hexose residues, maltose, dihexosan, (Ber. **57**, 887), amylobiose (Ber. **57**, 1593), whereas amylopectin yields products containing three hexose residues, trihexosan (Ber. **57**, 887), amylotriose (Ber. **57**, 1581), hexatriose (J.C.S. **123**, 2666). The attack by pure enzyme preparations has been more successful than purely chemical methods.

2. **Paramylum,** $(C_6H_{10}O_5)_n$, occurs in the infusoria *Euglena viridis.* It gives no colour with iodine and is soluble in potassium hydroxide.

3. *iso***Lichenin,** *moss starch,* $(C_4H_{10}O_5)_n$, occurs in many lichens associated with lichenin (lichen cellulose) and in Iceland Moss, *Cetraria islandica.* It is coloured a dirty blue by iodine and yields glucose on hydrolysis. Preparation, see Ber. **57**, 1594. It closely resembles amylose in its degradations.

4. **Glycogen,** *liver starch,* $(C_6H_{10}O_5)_n$, is the principal reserve carbohydrate of mammals, and is laid down principally in the liver and muscles. It also occurs in lower animals, and in some plants (mushrooms). Glycogen is formed in the liver under normal conditions from glucose and certain other monoses, from glycerol, and from some of the amino-acids derived from proteins. On acid hydrolysis it yields glucose, with certain enzymes, maltose. In its reactions, it resembles electrolyte-free amylopectin (erythroamylose). It is coloured wine-red with iodine, and does not form a paste. Haworth and Percival (J.C.S. **1932**, 2277) suggest that the constitution of glycogen can be represented by a chain of about twelve glucose residues, linked together as in maltose. This is based on the isolation of about 9% of 2 : 3 : 4 : 6-tetramethylglucose together with trimethylglucose by the hydrolysis of methylated glycogen. The tetramethylglucose is derived from the glucose residue at one end of the chain.

5. **Inulin** is the reserve carbohydrate of certain plants such as dahlias, chicory and certain compositæ. It differs from the polysaccharides referred to above in that it yields fructose instead of glucose on hydrolysis. The fructose residues in inulin are the unstable fructofuranose, but the sugar reverts immediately on isolation to the normal fructopyranose (J.C.S. **1928**, 519). As regards the molecular complexity of the substance, ebullioscopic determinations on purified inulin lead to a formula containing at least 20 fructofuranose units (J.C.S. **1928**, 2691), whereas determinations of the molecular weight of triacetylinulin (Ber. **54**, 1281 : **55**, 1409) or of trimethylinulin (Helv. Chim. Acta. **4**, 249) lead to lower values, the molecule containing only 9 fructose units. It is probable that the higher value is more accurate.

Inulin is soluble in water, has $[\alpha]_D - 36°$ and does not give any colour with iodine. The *triacetate,* insoluble in water, has $[\alpha]_D^{20} - 42{\cdot}5°$.

6. **Carubin** occurs in St. John's Bread, the pods of *Ceratonia siliqua,* and is hydrolysed by acids to yield mannose.

Dextrin.—*Starch gum, leiocome,* $(C_6H_{10}O_5)_n$. This term is applied to a number of substances obtained as intermediate products in the conversion of starch to maltose and glucose. They are obtained by the depolymerization of starch in various ways, *e.g.* by heating starch alone to 160–200° or by the action of dilute sulphuric acid. Various dextrins have been described, *amylodextrin, erythrodextrin,* which gives a red colour with iodine, and *achroodextrin,* which no longer gives any iodine colour. These various dextrins are not very definitely characterized (Ber. **28**, R. 987 : **29**, R. 41 : C. 1897, I. 408 : Ann. **309**, 288). The dextrins are readily soluble in water and are precipitated by alcohol. They form gummy amorphous masses and their aqueous solutions are dextrorotatory, whence their name. They do not reduce Fehling's solution, and are not directly fermentable: in the presence of diastase they can be fermented by yeast, after a preliminary conversion to glucose. They yield glucose on hydrolysis with acids. They react with phenylhydrazine (Ber. **26**, 2933). A gum has been isolated from yeast cells (Ber. **27**, 925 : **60**, 1639, 1644).

Dextrin is manufactured on the large scale as a substitute for gum by moistening starch with 2% nitric acid, allowing it to dry in air and then heating it at 110° (Ber. **23**, 2104).

A depolymerization product of inulin analogous to the dextrins has been isolated by Drew and Haworth, and named inulin "*lævulin*" (J.C.S. **1928**, 2695).

Cellulose,* *lignose*, $(C_6H_{10}O_5)_n$, forms the principal component of the cell walls of plants. X-ray spectroscopy has shown that cellulose has a crystalline structure and forms long thread-like crystals of the rhombic system (Ber. **53**, 2162 : Z. Physik. **3**, 342 : **7**, 147 : Naturwissenschaften, **9**, 288 : Ber. **61**, 593). Cellulose resembles starch in many ways, but on account of its purpose as a supporting substance is much tougher. Cellulose is accompanied by lignin as a supporting substance. Pine, for example, contains 58% cellulose and 30% lignin ; oak, 39% cellulose and 26% lignin. To obtain pure cellulose, vegetable fibre, or, better, cotton-wool is treated successively with dilute potassium hydroxide solution, dilute hydrochloric acid, water, alcohol, and ether, to remove all admixtures (encrusting substances). Cellulose remains then as a white, amorphous mass. So-called "Swedish filter paper" consists of nearly pure cellulose.

Sulphite cellulose is prepared by treating wood with hot calcium bisulphite liquor under pressure, whereby the lignin surrounding the wood fibre is dissolved. Sodium cellulose is formed when straw is heated with sodium hydroxide solution. Cellulose is employed for the manufacture of paper, parchment paper, gun-cotton, smokeless powder, celluloid and celluloid-like bodies, artificial silk, etc.

Cellulose is insoluble in most of the usual solvents, but dissolves without change in an ammoniacal copper solution (Ber. **38**, 2798 : **44**, 3320 : **54**, 3220 : **55**, 1899). Acids, various salts of the alkalis and sugar precipitate it as a gelatinous mass from such a solution. After washing with alcohol it is a white, amorphous powder. According to Hess (Ann. **435**, 1), this consists of unchanged cellulose.

Derivatives of Cellulose.—When cellulose is treated with alkali of various concentration, it undergoes physical change with the formation of a so-called *hydrate-cellulose*. This treatment is of importance in the commercial process of mercerization (Ber. **40**, 441, 4903). (Effect of mercerization on the X-ray structure of cellulose, Ber. **61**, 600.) Similarly, by the action of dilute acids or oxidizing agents (nitric acid, bleaching powder, permanganate, hydrogen peroxide) the hydro- or *oxy-celluloses* are formed. In both the cellulose has undergone chemical alteration, and the compounds have some reducing action on Fehling's solution, and are converted by quicklime into *iso*saccharinic acids. The oxycelluloses which are not pure compounds contain carboxyl groups.

Degradation of Cellulose.—1. *Acid hydrolysis.* Strong mineral acids break down cellulose with a 100% yield of glucose. This forms the basis of manufacture of wood spirit.

2. *Bacterial breakdown.*—Enzymes which attack cellulose (*cellulases*) have hitherto only been found in bacteria (Z. physiol. Chem. **78**, 266). The only identifiable intermediate product is the disaccharide cellobiose. Bacterial action has shed little light on the constitution of cellulose, as in practice cellulose is usually completely oxidized to CO_2 and water and in other cases only the lower fatty acids have been isolated.

3. *Acetolysis.*—Franchimont in 1879 (Ber. **12**, 1941) obtained by the action

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* K. Hess, Cellulosechemie, Leipzig, 1928, Akad. Verl.-Ges. E. Heuser Lehrbuch der Cellulosechemie, 2. Aufl. Berlin, 1923.

of acetic anhydride and concentrated sulphuric acid on cellulose the octaacetate of the disaccharide cellobiose. Karrer (Helv. Chim. Acta. **4**, 174) and Freudenberg (Ber. **54**, 767) have shown that in cellulose at least 60% of cellobiose is preformed. Cellobiose is related to cellulose as maltose is to starch (Ber. **34**, 1115: C. 1902, I. 183: *cf.* 1901, II. 405).

Hess (Ber. **54**, 2867) has obtained the hexaacetate of a biose anhydride which shows a great tendency to association.

A cello*iso*biose has been described as another disaccharide obtained in the acetolytic breakdown of cellulose (Z. angew. Chem. **33**, 100), but its existence has recently been denied (J.C.S. **1932**, 2368).

By the action of acetic anhydride and a little sulphuric acid at 0° there is obtained together with octaacetylcellobiose, a so-called *cellulose dextrin* (Z. physiol. Chem. **105**, 173).

4. *Distillation in vacuo.*—By the distillation of cellulose in vacuo, up to 35% of lævoglucosan is formed (Helv. Chim. Acta. **1**, 87). Karrer has shown that this is only obtained from β-glucose, so that its formation is evidence for the existence of β-glucose residues in cellulose.

5. *Methylation of Cellulose.*—A trimethylcellulose was obtained in 1921 (J.C.S. **119**, 77) using repeated applications of methyl sulphate and alkali. A fully methylated cellulose was obtained in one operation (J.C.S. **1932**, 2270) by the action of methyl sulphate and alkali on a specially prepared acetone-soluble acetylcellulose.

Constitution of Cellulose.—Few natural products have had so many formulæ speculatively assigned to them as cellulose (*cf. Pringsheim*, Die Polysaccharide, 2. Aufl. 1923, pp. 217 *et seq.*). None of them has survived experimental verification. More recent work has not brought the matter to an entirely satisfactory solution. According to one school, cellulose is composed of basal molecules of relatively low molecular weight, joined together by subsidiary valencies (Lattice-forces). For the basal substance, on the results of the hydrolysis of trimethylcellulose, an anhydro-trisaccharide has been advocated by English investigators (Irvine and Hirst, J.C.S. **123**, 518); while from the behaviour of cellulose in cuprammonium solutions (Ann. **435**, 7) or from the cryoscopic behaviour of crystalline acetylcellulose (Ann. **448**, 99) a simple glucose anhydride is postulated. This view is contradicted by the purely structural view of cellulose, in which it is regarded as constituted of numerous glucose residues linked together in a cellobiose-like manner. This view receives its main experimental support in the formation of cellobiose by the acetolytic breakdown of cellulose (*q.v.*: Ann. **460**, 288). This view is confirmed by X-ray spectroscopy of cellulose fibres, the results showing that in the cellulose " crystal " some 40 glucose residues are joined by a cellobiose linkage and arranged spirally round a long axis. 40–60 of such chains associate together by micellar forces to form a cellulose particle (K. B. Meyer and H. Mark, Ber. **61**, 612). Haworth and Machemer (J.C.S. **1932**, 2270), on the results of hydrolysis of fully methylated cellulose, conclude that the cellulose molecule is composed of upwards of 100–200 β-glucopyranose residues linked in the 1 : 4-positions.

Technically important derivatives of cellulose.

Wood Alcohol.—Obtained (*a*) from the sulphite-lye of cellulose manufacture, which contains sugar derived from the hemicelluloses of wood: this can be fermented to yield alcohol: 11–17 litres of alcohol are obtained per ton of dry wood. (*b*) Sawdust is partially hydrolysed to sugars by rapid heating under pressure with dilute acids, the hemicelluloses again being the principal source of the sugar which is then fermented to yield alcohol.

Nitrocelluloses.

Strong nitric acid produces from cellulose, first, a hydrolysable *nitrate* (Ber. **37**, 349: C. 1908, I. 2024). A more concentrated acid, or, better, a mixture of nitric and sulphuric acids forms nitric esters, known as *nitrocellulose* (C. 1901, II. 34, 92: Ber. **34**, 2496).

According to the mode of action, the products show varying characteristics. If pure cotton wool is immersed for 3–10 minutes in a cold mixture of 1 part of nitric acid with 2–3 sulphuric acid, and then carefully washed with water, there is formed *gun-cotton* (pyroxylin), which was discovered in 1845 by Schönbein. It is insoluble in alcohol and ether and their mixture, and explodes violently when ignited in a closed space by percussion. In the air it burns very rapidly without exploding. If the cotton wool be immersed for a longer time in a warm mixture of 20 parts of powdered sodium nitrate and 30 of concentrated sulphuric acid, there is formed *soluble pyroxylin*, which is dissolved by a mixture of ether and a little alcohol. The solution is known as *collodion* ; this, on evaporation, leaves the pyroxylin in the form of a thin transparent skin insoluble in water, which is employed in surgery and photography.

Chardonnet obtained *artificial silk* by denitrifying thin fibres of collodion by means of ammonium sulphide.

The explosive insoluble gun-cotton consists mainly of *cellulose hexanitrate*, $C_{12}H_{14}(O{\cdot}NO_2)_6O_4$, whilst the ether-alcohol soluble pyroxylin is formed chiefly of the *tetranitrate*, $C_{12}H_{16}(ONO_2)\ O_6$, and the *pentanitrate*, $C_{12}H_{15}(O{\cdot}NO_2)_5O_5$ (Ber. **13**, 186). The solution of collodion cotton in nitroglycerine (with small quantities of other substances), constitutes a blasting gelatin which is employed as *smokeless powder* (Ber. **27**, R. 337).

When mixed with camphor, nitrocellulose forms *celluloid*, a substance like *vulcanite* (highly vulcanized rubber), having the disadvantage of burning violently when ignited.

Esters of Organic Acids.—*Acetylcellulose* is formed by the action of glacial acetic acid, acetic anhydride, and a small quantity of concentrated sulphuric acid, or zinc chloride on cellulose (Crystal structure, see Ann. **444**, 284). It is characterized by its solubility in various organic solvents and insolubility in water. It is used, like ammonium-copper hydroxide cellulose (p. 734) and nitrocellulose, for the preparation of artificial silk, and many other technical purposes (C. 1902, II. 1022 : 1907, I. 1736 : 1908, I. 1831).

Simultaneous action of acetic anhydride and nitric acid produces *cellulose acetonitrate* (Ber. **41**, 1837). Formic acid and sulphuric or hydrochloric acid give rise to *cellulose formate* (C. 1908, I. 328). Benzoyl chloride and pyridine produce *benzoyl cellulose* (C. 1903, I. 744).

Xanthogenates.—Cellulose is dissolved by strong alkalis and carbon bisulphide in the form of a xanthogenic ester :

$$(C_6H_9O_4{\cdot}O{\cdot}CS{\cdot}SNa,\ NaOH)_n.$$

This solution, after a ripening process (*viscose*), is used for the preparation of artificial silk.

Hemicelluloses.—The hemicelluloses accompany cellulose constantly, and share with it its property as a supporting substance. They have, however, a further use as reserve carbohydrate, their more ready hydrolysis by acids and enzymes making them suitable for this purpose. The hemicelluloses are divided into *hexosans*, which yield on hydrolysis hexoses, and *pentosans*, which yield pentoses on hydrolysis.

According to the nature of the sugar formed on hydrolysis, the hexosans are further subdivided into *mannans* (reserve carbohydrate of palms and St. John's Bread (see Carubin)) and *galactans*, which occur in the seeds of lupins, lucerne and beans. The substance *agar-agar* used in bacterial culture media is related to the galactans. The pentosans can be similarly subdivided into *xylans* and *arabans*.

The vegetable gums belong to this class of substances.

Arabin, gum, exudes from many plants, and solidifies to a transparent, glassy, amorphous mass, which dissolves in water to a clear solution. *Gum arabic* or *gum Senegal* consists of the potassium and calcium salts of *arabic acid*. The latter can be obtained pure by adding hydrochloric acid and alcohol to the solution. It is then precipitated as a white, amorphous mass, which becomes glassy at 100°, and possesses the composition $(C_6H_{10}O_5)_2 + H_2O$. It forms compounds with nearly all the bases, which dissolve readily in water.

Some varieties of gum, *e.g.* gum arabic, yield galactose in considerable quantity when boiled with dilute sulphuric acid ; and with nitric acid they are converted into mucic acid ; others, like *cherry gum*, are transformed on boiling with sulphuric acid into *l*-arabinose, $C_5H_{10}O_5$ (p. 674), and into oxalic acid, not mucic acid, by nitric acid. The gum, extracted from beechwood by alkalis and precipitation with acids, is converted into xylose (p. 674) by hydrolysis (J. pr. Chem. **103**, 69).

Bassorin, *mucilage*, constitutes the chief ingredient of *gum tragacanth*, *Bassora gum*, and of *cherry* and *plum gums* (which last also contain arabin). It swells up in water, forming a mucilaginous liquid, which cannot be filtered; it dissolves very readily in alkalis. On the hydrolysis of plant-mucus, see Ber. **36**, 3197.

Pectin substances (from πηκτός, coagulated) occur in fruit juices, *e.g.*, apple, cherries, currants, greengages, etc. They cause these, under suitable conditions, to gelatinize. They are closely allied to the vegetable gums, and may be regarded as oxymucilage (Ann. **286**, 278: Ber. **28**, 2609).

The basic constituent of the pectin substances is the calcium or magnesium salt of pectic acid, which is probably constituted by 4 molecules of galacturonic acid, 1 of galactose and 1 of arabinose joined in a six-sided ring (Nanji, Paton and Ling, J. Soc. Chem. Ind. 1925, **44**, 253T). (Recent summary of the constitution of the pectin substances, see Ehrlich, Z. angew. Chem. 1927, **40**, 1305).

Lignin.*—Little is at present known about this substance, which accompanies cellulose in wood. The lignin content of wood is 20–30%. Lignin can be prepared, according to Willstätter and Zechmeister (Ber. **46**, 2401), by the action of hydrochloric acid (saturated at 0°) (40%) on sawdust at room temperature. Lignin remains unattacked. Further methods of preparation, see Z. angew. Chem. 1924, **37**, 169.

Lignin is converted by the action of sulphurous acid or concentrated bisulphite solution into a sulphonic acid, whose barium and calcium salts have been investigated (Ber. **53**, 707). Chlorine dioxide is a good solvent for vegetable encrustations, among which is included lignin (Schmidt, Ber. **54**, 1860: **56**, 23). Lignin gives an intensive red colour with the alcoholic or aqueous solution of certain phenols (especially with phloroglucinol) in presence of hydrochloric acid.

Lignin is not a chemical individual. Its analytical figures vary from those required for $C_{18}H_{24}O_{10}$ to those of $C_{40}H_{45}O_{18}$. The presence of hydroxyl, methoxyl and acetyl groups is certain: that of carboxyl, keto- or aldehydic groups more doubtful. It cannot be said with certainty whether lignin contains an aromatic nucleus, or whether it is purely aliphatic in structure.

F. NITROGEN-CONTAINING POLYSACCHARIDES

Chitin, which forms the principal constituent of the shells of crabs, lobsters and other crustacea, is a representative of these compounds. According to Krawkow (Z. Biol. **29**, 177) chitin in the shell is combined with protein and occurs in various modifications. The nitrogen in chitin occurs in the form of a partially acetylated chitosamine (*d*-glucosamine) (*q.v.*) and on hydrolysis of chitin with hydrochloric acid, *d*-glucosamine and acetic acid are formed (*Ledderhose*, Z. physiol. Chem. **2**, 224):

$$\underset{\text{Chitin.}}{C_{18}H_{30}N_2O_{12}} + 4H_2O = \underset{\text{Chitosamine.}}{2C_6H_{13}NO_5} + \underset{\text{Acetic acid.}}{3CH_3CO_2H.}$$

Chitin is insoluble in water or in Schweitzer's reagent. It has optical rotatory power of − 14·1, rising to + 56. Heating with alkali produces chitosan, whose hydrochloride has been obtained crystalline. The action of nitrous acid produces *chitose*, $C_6H_{10}O_5$, which is probably a 2 : 5-anhydromannose (C. 1921, I. 614: see p. 699). Chitin is very resistant to enzymes.

Constitution.—The linking of the acetylated glucosamine residues is effected through the nitrogen atoms. Karrer and Smirnoff (Helv. Chim. Acta. **5**, 832) obtained by distillation with zinc dust *chitopyrrole*, which they identified as 2-methyl-1-*n*-hexylpyrrole. This mode of linkage represents chitin as intermediate between the proteins

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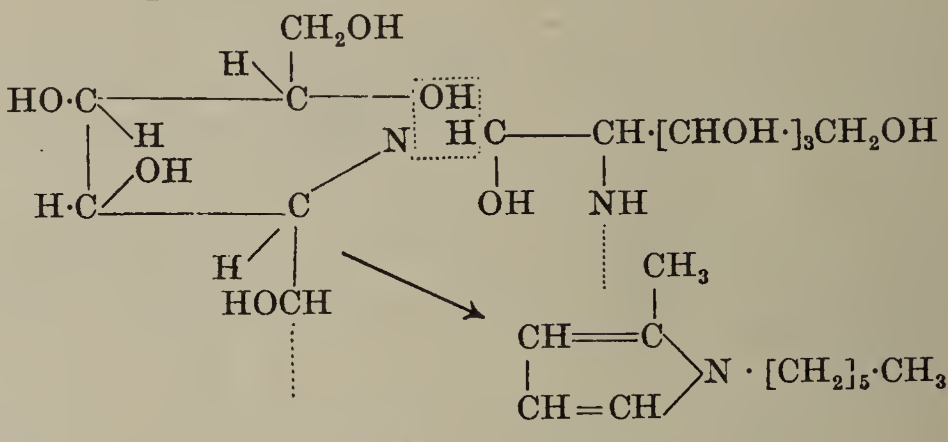
* W. Fuchs, Die Chemie des Lignins, Berlin, 1926, Springer.

and carbohydrates. The transformation of a chitin fragment into chitopyrrole is represented as follows (acetyl groups omitted):



······· = Linkage of next glucosamine residue.

The skeletal substance of fungi is probably identical with chitin, and the *mycosin* obtained from it by the action of alkali identical with chitosan (Ber. **28**, 821: R. 476: C. 1908, II. 2016).

Lycoperdin, which on hydrolysis yields 2 mols. of glucosamine and 1 mol. formic acid, belongs to the same class.

Chondroitinsulphuric acid is a compound obtained from cartilage and mucins. On complete hydrolysis, it yields, through a series of intermediate compounds (chondroitin, chondrosin), the following components: 2 mols. glucosamine, 2 mols. glycuronic acid, 2 mols. acetic acid, 1 mol. hexose and 2 mols. acetic acid. One acetyl group is definitely attached to nitrogen. For the mode of linkage of the various components, see Levene (C. 1915, I. 1127) and Schmiedeberg (C. 1920, III. 636).

Mucoidinsulphuric acid, see C. 1919, I. 473.

Pneumococcus Polysaccharides.—Another important nitrogen-containing polysaccharide is that obtained from Type I *pneumococcus*, which contains C 43·3%, H 5·8%, N 5·0%, amino-N 2·5% and has $[\alpha]_D$ + 300°. It yields galacturonic acid and an amino-sugar on hydrolysis. Types II and III pneumococci also yield polysaccharides, but these are nitrogen-free. These compounds have been chiefly investigated by Heidelberger, Avery and co-workers (see Chem. Reviews, 1927, **3**, 403, and various papers in J. Experimental Med. and J. Biol. Chem.).

SUBSTANCES OF PHYSIOLOGICAL IMPORTANCE OF PARTIALLY KNOWN CONSTITUTION

A number of substances will be briefly dealt with here, which from their nature belong to the borderland between Organic and Physiological Chemistry, and which have already been frequently referred to in the systematic parts of this book. Among them may be mentioned the proteins, the nucleic acids, the sterols, the bile acids, the enzymes, etc.

Proteins

Literature :—*E. Fischer*, Untersuchungen über Aminosäuren, Polypeptide und Proteine, 1906 (Springer) : *Hammarsten*, Lehrbuch der Physiologischen Chemie, 9. Aufl. 1922 : *Jordan Lloyd*, Chemistry of Proteins, London, 1926 : *C. Oppenheimer*, Der gegenwärtige Stand der Eiweissforschung, Therapie der Gegenwart, 1926, **67**, 27 : *M. Bergmann*, Allgemeine Strukturchemie der komplexen Kohlenhydrate und der Proteine (Ber. **59**, 2973) : *E. Waldschmidt-Leitz*, Zur Struktur der Proteine (Ber. **59**, 3000) : *O. Kestner*, Chemie der Eiweisskörper, 4. Aufl. 1925 : *S. Edlbacher*, Die Strukturchemie der Aminosäuren und Eiweiss körper, Leipzig, 1926.

The proteins form an important component of every living cell. The complete synthesis of a protein from CO_2, H_2O, NH_3, HNO_3 and H_2SO_4 is confined to vegetable cells : the animal organism is capable of a partial synthesis from amino-acids.

The general composition of the different proteins varies within definite limits (J. pr. Chem. [2] **44**, 345).

C . . .	50–55%
H . . .	6·9–7·3%
N . . .	15–19%
O . . .	19–24%
S . . .	0·3–2·4%
Ash . . .	A trace

Colour Reactions.—The proteins give characteristic colour reactions, by which they can be recognized. These colour reactions are not, however, confined to the proteins, but are also given by some of their constituent amino-acids.

Millons Reaction.—When warmed with a mercuric nitrate solution containing a trace of nitrous acid all proteins give a red colour, similarly to tyrosine.

Xanthoproteic Reaction.—When warmed with nitric acid a yellow colour is produced, which ammonia converts into golden-yellow.

Biuret Reaction.—Protein solutions give with copper sulphate and potassium hydroxide red to violet colorations. This reaction is not, however, specific for proteins, but is given by various other compounds (Ber. **29**, 1354).

Ninhydrin Reaction.—Proteins give a blue colour when treated with triketohydrindene hydrate.

Other Colour Reactions.—When heated with fuming hydrochloric acid proteins give beautiful violet colours. When treated with a sugar solution and concentrated sulphuric acid, a red colour is produced which darkens on exposure to air. If the solution of a protein in glacial acetic acid is treated with concentrated sulphuric acid, a violet solution is produced which shows characteristic absorption bands.

Solubility.—The proteins in general are insoluble in water and owe their solubility in the fluids of the living organisms to the presence of salts and partly to other unknown substances. They are insoluble in alcohol and ether. Many proteins have been obtained crystalline: egg albumin, for example, is precipitated in the crystalline form from its solution by the action of ammonium sulphate (Z. physiol. Chem. **130**, 72): the crystalline structure of silk protein can be demonstrated by Debye's X-ray spectrographic method (Ber. **53**, 2162: Z. physiol. Chem. **141**, 158).

Precipitation Reactions.—Proteins are precipitated from their aqueous solution by alcohol. In general, a change in the state of the protein occurs in this process, and it loses its solubility in water (*denaturation*).

Similarly, proteins can be precipitated from their aqueous solutions by the action of metallic salts, this depending upon the formation of molecular compounds between the salt and constituents of the protein. Two types of salt precipitation are to be distinguished:

(*a*) *Reversible precipitation, i.e.* where the solubility of the protein in water is retained, by sodium sulphate, magnesium sulphate and ammonium sulphate.

(*b*) *Irreversible precipitation*, particularly produced by the salts of heavy metals.

Finally, acids precipitate proteins, with simultaneous denaturation. Mineral acids, particularly nitric acid, have this property, as have also certain complex inorganic acids such as phosphotungstic acid, phosphomolybdic acid, potassium mercuri- and bismuthi-iodides, acetic acid with tannic or picric acids, trichloroacetic acid, salicylsulphonic acid, taurocholic acid, nucleic acid and chondroitinsulphuric acid, or acetic acid and potassium ferrocyanide.

The precipitation of proteins is also brought about by heat coagulation.

Proteins are typical amphoteric compounds, *i.e.*, they are capable of forming both cations and anions in aqueous solution. The hydrogen ion concentration where equal amounts of protein are ionized as cation and anion is designated the *isoelectric point*. The isoelectric point is given by the equation

$$[\mathrm{H}] = \frac{k_a}{k_b} \cdot k_w$$

where k_a and k_b are the acid and basic dissociation constants of the protein and k_w the dissociation constant of water.

The isoelectric point, which is an individual characteristic of a protein, can be determined by various physicochemical methods. At it

(*a*) the viscosity of a protein solution is a minimum;
(*b*) the migration of protein ions in an electric field ceases;
(*c*) the swelling of the protein is minimal;
(*d*) the precipitability by alcohol is maximal.

Altered Proteins.—Acid albumin and alkali albuminate are products, comparatively little investigated, formed from proteins by the gentle action of acids or alkalis. They are only slightly altered proteins. Acid albumins are soluble in dilute acids. Alkali albuminates are strong acids, reacting with calcium carbonate with production of CO_2.

Degradation of Proteins.—(1) By the *oxidation* of proteins volatile fatty acids, aldehydes, ketones, nitriles, hydrocyanic acid and benzoic acid have been obtained. Gentle oxidation with hypobromite at 0° appears to be of value in constitutional investigations (Ber. **58**, 1346).

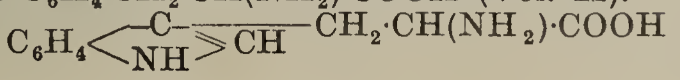
(2) *Hydrolysis*—This method of protein degradation, which takes place by the addition of the elements of water, is brought about by heating with dilute mineral acids or by the action of proteolytic enzymes such as pepsin, trypsin, erepsin, papain, etc. (*q.v.*). The degradation proceeds through a series of intermediate substances (peptones, polypeptides and dipeptides) eventually to complete breakdown to amino-acids. With purified enzymes and under very definite conditions with mineral acids (Z. physiol. Chem. **129**, 106) it is possible to isolate definite intermediate products (Ber. **40**, 3544: Z. physiol. Chem. **156**, 68) which are of the greatest importance in the determination of protein constitution.

The separation of the mixture of amino-acids obtained by one or other of the above methods is carried out by Fischer's ester method, where the amino-acids are esterified and the esters fractionated in vacuo, or by Dakin's more recent method (Biochem. J. **12**, 290: **13**, 398: J. Biol. Chem. **44**, 499). In this method the monoamino-acids and some peptide anhydrides are extracted from the aqueous hydrolysate by a suitable partially miscible solvent, such as butyl alcohol: the diamino-acids and dicarboxylic acids remain behind and can then be separated. The so-called hexone bases, arginine, lysine and histidine, can be precipitated together by phosphotungstic acid.

Products of Protein Hydrolysis.

The amino-acids obtained by complete hydrolysis of proteins are collected in the following table:

(*a*) *Monoamino-monocarboxylic Acids.*

Glycine, $NH_2{\cdot}CH_2{\cdot}COOH$. Hippuric acid, $C_6H_5CO{\cdot}NH{\cdot}CH_2{\cdot}COOH$ (Vol. II).
Alanine, $CH_3{\cdot}CH(NH_2){\cdot}COOH$.
Valine, $(CH_3)_2CH{\cdot}CH(NH_2){\cdot}COOH$.
Leucine, $(CH_3)_2CH{\cdot}CH_2{\cdot}CH(NH_2){\cdot}COOH$.
*iso*Leucine, $C_2H_5{\cdot}CH(CH_3){\cdot}CH(NH_2){\cdot}COOH$.
Phenylalanine, $C_6H_5{\cdot}CH_2{\cdot}CH(NH_2){\cdot}COOH$ (Vol. II).
Tyrosine, $HO{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH(NH_2){\cdot}COOH$ (Vol. II).
Tryptophan, 

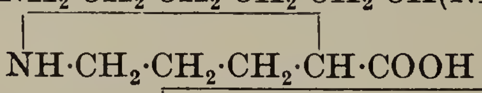
$C_6H_4\left<\begin{array}{l}\text{C}\text{———}CH_2{\cdot}CH(NH_2){\cdot}COOH\\ \text{NH}{\geqslant}\text{CH}\end{array}\right.$ (Vol. II).

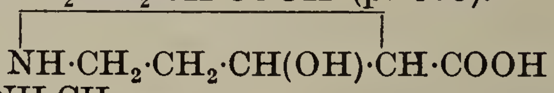
(*b*) *Monoamino-dicarboxylic Acids*

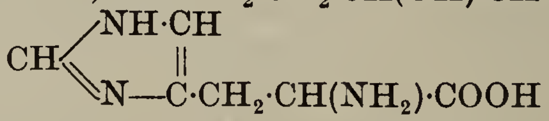
Aspartic acid, $HOCO\cdot CH(NH_2)\cdot CH_2\cdot COOH$.
Glutamic acid, $HOCO\cdot CH(NH_2)\cdot CH_2\cdot CH_2\cdot COOH$.
Hydroxyglutamic acid, $HOCO\cdot CH(NH_2)\cdot CH(OH)\cdot CH_2\cdot COOH$.

(*c*) *Hydroxyamino-, Thioamino-, Diamino- and Imino-Acids*

Serine, $HOCH_2\cdot CH(NH_2)\cdot COOH$ (p. 595).
Cystine, $[\cdot S\cdot CH_2\cdot CH(NH_2)\cdot COOH]_2$ (p. 597).
Methionine, $CH_3\cdot S\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot COOH$ (p. 597).
Ornithine, $NH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot COOH$: also arginine, $NH_2C(:NH)\cdot NH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)COOH$, and ornithuric acid, $C_6H_5CO\cdot NH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot COOH$ (p. 598).
Lysine, $NH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot COOH$ (p. 598).

Proline, 
$\overline{NH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH}\cdot COOH$ (p. 598).

Hydroxyproline, 
$\overline{NH\cdot CH_2\cdot CH_2\cdot CH(OH)\cdot CH}\cdot COOH$ (p. 652).

Histidine, 
(Vol. III).

All these compounds are not contained in every protein and their relative quantities in the various proteins fluctuate within very wide limits : in addition, the hydrolysis products are not recovered quantitatively by any hydrolysis method (p. 741). The results of the hydrolysis of gelatin are demonstrated in the following table (Dakin, J. Biol. Chem. **44**, 499) :

Glycine	25·5%	Hydroxyproline	14·1%
Alanine	8·7%	Aspartic acid	3·4%
Leucine	7·1%	Glutamic acid	5·8%
Serine	0·4%	Histidine	0·9%
Phenylalanine	1·4%	Arginine	8·2%
Tyrosine	0·01%	Lysine	5·4%
Proline	9·5%	NH_3	0·4%

(3) **Putrefaction.**—From the products of putrefaction of proteins caused by micro-organisms, bacteria, etc., can be isolated the fatty acids up to caproic acid, phenylacetic acid, $C_6H_5\cdot CH_2\cdot COOH$ (Vol. II), phenol, C_6H_5OH (Vol. II), and indolepropionic acid, indoleacetic acid, skatole (2-methylindole), indole, compounds which are formed from tryptophan in a similar manner to the formation of the previously mentioned acids from phenylalanine and tyrosine. (Formulæ above : see also Ber. **37,** 1801 : **40,** 3029.) In addition, various basic compounds, principally aliphatic diamines and imines, are formed, and are often referred to as ptomains.

Certain pathogenic micro-organisms such as the diphtheria bacillus, bring about a less far-reaching decomposition with the formation of poisonous protein- or peptone-like compounds, known as toxins or toxalbumins. These lose their toxicity when solutions of them are heated (Ber. **23,** R. 251).

Constitution of Proteins.—In spite of much research the constitution of the proteins has not yet been solved.

Molecular weight determinations are surrounded with many difficulties, and the molecular weights of the simple proteins calculated indirectly from their sulphur contents, or of the conjugated proteins from their iron contents, afford values which do not agree satisfactorily with the determinations by the freezing-point method. Proteins obviously have very large molecules, as demonstrated by the great number of amino-acids which can be obtained by their hydrolysis.*

The mode of linkage of the nitrogen is of great importance in the consideration of protein structure. By nitrous acid only some 4–5% of the nitrogen is liberated (Van Slyke's method, Ber. **43**, 3170): this is the nitrogen present in the form of free amino groups. The free NH_2-groups of the amino-acids, the end products of protein hydrolysis, are therefore not preformed in the natural protein, but are set free during the hydrolysis. The greater part of the protein nitrogen must be linked as secondary and tertiary nitrogen atoms. Emil Fischer has put forward the idea that the amino-acids are linked together in an acid-amide-like so-called peptide manner: *i.e.*:

$$—CO—NH— \quad \text{or} \quad —C(OH)=N—.$$

The confirmation of this view is given by the isolation of di- and polypeptides by gentle protein hydrolysis (p. 741) and by the splitting of synthetic peptides by proteases.

The existence of this type of linkage in di-, tri- and polypeptides as the sole mode of linkage is substantiated by the use of the purified enzyme erepsin, an enzyme which attacks exclusively this type of linkage, even in a solution of a dipeptide (Ber. **61**, 300). With the transition of the dipeptides, *via* the polypeptides and the ill-defined peptones to natural proteins, another type of constitution, whose nature at present is unknown, makes its appearance. Neither proteins nor peptones are attacked by erepsin, which would be expected if a peptide-link was the sole basis for the building up of proteins. Contrariwise, no dipeptide is split by trypsin (Naturwissenschaften, **14**, 131).

Various views have been put forward as to the nature of this other mode of linkage. In particular, the existence of cyclic linkages has been advocated, a view which receives support in the isolation from proteins of various heterocyclic ring compounds. Among these are: *diketopiperazines* (*Abderhalden*, Z. physiol. Chem. **139**, 182: Naturwissenschaften, **12**, 716): *oxazines* (*Bergmann*, Z. physiol. Chem. **140**, 128: Naturwissenschaften, **12**, 1155): *pyrazines*, (*Karrer*, Helv. Chim. Acta. **6**, 1108): *hydroxypyrroles* (*Troensgaard*, Z. physiol. Chem. **112**, 86: **127**, 137: **133**, 116). Nevertheless, these types of compound do not seem to be of great importance in the structure of natural protein, on the one hand because they are formed under conditions which fairly certainly permit of atomic migrations with secondary ring closure (*cf.* Ber. **56**, 1887), and on the other hand because none of these cyclic types are hydrolysed by purified proteases. It would therefore appear that, at any rate among the proteins readily attacked by enzymes, that this type of ring-linkage cannot play an important part.

The conception introduced by analogy from the chemistry of starch and cellulose, that protein is built up of comparatively simple molecules joined by subsidiary valencies to form the great protein molecule, has also not received universal recognition, although there is experimental support for this conception in the X-ray structure of silk protein (Ber. **53**, 2162) and in the tendency of simple

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* The molecular weight of hæmoglobin has been found to be about 68,000 by three entirely different methods, osmotic pressure (*Adair*, Proc. Roy. Soc. [B] **98**, 523), sedimentation rate of hæmoglobin in a high-speed centrifuge (*Svedberg*, Z. physik. Chem. 1927, **127**, 51: Nature, 1929, **123**, 871) and diffusion coefficient of carbon-monoxide-hæmoglobin (*Northrop* and *Anson*, J. Gen. Physiol. 1929, **12**, 543). Certain other chromoproteins appear to have even higher molecular weights.

cyclic models to association (Ann. **445**, 17). The conception of associated basal compounds in the protein molecule, however, receives no support in the more recent results of enzyme action, using improved analytical and preparative methods (Z. physiol. Chem. **156**, 80).

Enzyme research is, however, shedding some light on the nature of this linkage. As already mentioned, the problems of protein constitution and of the cause of the extraordinary specificity of the proteases are closely related. More recent results with di-, tri- and polypeptides (Ber. **60**, 1906 : **61**, 299) show that the specific activity of the individual proteases (erepsin, trypsin, trypsin-kinase) is not so much to be referred to the attack by each enzyme of a specific linking in the protein molecule as that " the specificity of pancreatic trypsin and intestinal erepsin are conditioned by the nature of the amino-acid components as well as by the length of the peptide chain " (*Waldschmidt-Leitz,* Ber. **61**, 300).

Fractional enzymatic hydrolysis with pure enzyme preparations and the identification of the intermediate products should yield the clue to a clear conception of the structure of proteins.

Physiology of Proteins.—The proteins ingested with food are hydrolysed by the united attack of trypsin, trypsin-kinase and erepsin through the intermediate stages of peptones and polypeptides to their constituent amino-acids. These are absorbed through the intestinal wall. In the tissues the reverse process takes place with the formation of various body proteins : these are being continuously broken down and renewed.

If an excess of protein is administered, the animal organism possesses no ability, as in the case of carbohydrates, to store it as such, but the protein is deaminated and subsequently stored as fat or carbohydrate.

The breakdown of protein in the body commences with an intracellular enzymatic breakdown to amino-acids, which after deamination are oxidized to carbon dioxide and water. The ammonia produced by deamination is rendered innocuous in the liver by being condensed with carbonic acid to form urea, which is excreted by the kidneys.

Classification of Proteins

The structure of the proteins is too imperfectly known to permit of a systematic classification. The proteins are subdivided largely by characteristics such as their solubility in water, precipitability, etc.

A. Simple Proteins

1. **Protamines.**—These are the simplest proteins, and were discovered by Miescher, and largely investigated by Kossel. They are composed of very few amino-acids and occur exclusively in the spermatozoa of certain fish. A characteristic of this class is the high content of arginine : *salmin* from the salmon and *clupein* from the herring are typical examples. The protamines are not attacked by pepsin, but are hydrolysed by trypsin or erepsin. Partial enzymatic hydrolysis of clupein, see Z. physiol. Chem. **156**, 68. By gentle acid hydrolysis are obtained the *protones* which stand to them in the same relationship as the peptones to the higher proteins.

2. **Histones.**—The best-known histone is that of the thymus gland (*Preparation,* Z. physiol. Chem. **157**, 81). It occurs in the gland combined with nucleic acid as *nucleohistone.* It is soluble in water and is precipitated from aqueous solution by alcohol. Histone is digested by pepsin-hydrochloric acid : from the products of hydrolysis a histopeptone can be isolated (Z. physiol. Chem. **49**, 301 : **119**, 66 : **120**, 94).

3. **Albumins** are soluble in water, in dilute acids and alkalis and in dilute or saturated neutral solutions of sodium chloride or magnesium sulphate. In the presence of acetic acid, albumins are completely precipitated by saturation with sodium chloride or magnesium or ammonium sulphate. When heated with sodium hydroxide, albumin yields a solution of the sodium salts of protalbinic acid, insoluble in water, and lysalbinic acid, soluble in water (Ber. **35**, 2195). Albumins, in presence of neutral salts, are coagulated by heat. *Serum-albumin* and *lactalbumin* are examples of the class: there are also many vegetable albumins.

4. **Globulins** are insoluble in water but soluble in dilute acids or alkalis, or dilute solutions of sodium chloride or magnesium sulphate. These solutions are coagulated by heat, but the globulin is precipitated without change, by saturation with ammonium or magnesium sulphate at 30°. *Myosin* and *musculin* (from muscles), *fibrinogen*, in blood plasma, which is converted by fibrin ferment into fibrin; *serum globulin* and *vitellin* are representatives. Certain globulins, which occur in vegetable seeds, such as *edestin*, which forms crystalline calcium and magnesium salts, have been investigated thoroughly. Other vegetable globulins include the *legumins*, *phaseolin* from beans, *conglutin* from lupins, etc.

5. **Prolamins.** (*Alcohol-soluble proteins.*) These are characterized by their physical properties. In a moist condition they consist of tough, doughy elastic masses. They occur in various grains, and are important factors in bread-making. Prolamins (glutens) are insoluble in distilled water, but are soluble in water containing a very little acid or alkali. A characteristic of the prolamins is their solubility in alcohol (60–70%).

Certain prolamins yield on hydrolysis large amounts of glutamic acid, but are deficient in the necessary amino-acids, lysine, cystine, tryptophan, in consequence of which they are incomplete as a source of protein. *Gliadin* from wheat, *hordenin* from barley, *zein* from maize are examples. The following amino-acids were obtained from zein (Z. physiol. Chem. **130**, 159):

Alanine	3·8%	Glutamic acid	31·3%
Leucine	25·0%	Aspartic acid	1·8%
Phenylalanine	7·6%	β-Hydroxyglutamic acid	2·5%
Proline	8·9%	Cystine and tryptophan absent.	

B. Scleroproteins. (*Derived from the intercellular substances*)

Certain nitrogenous substances, which form the greater part of the intercellular substance, and which when heated with water yield glue (gelatin), are referred to as collagen.

Gelatin swells in cold water, dissolves on heating to a viscous liquid, which on recooling solidifies to a gel. When heated with a little nitric acid, or by the action of strong acetic acid, the solution loses the property of gel-formation.

Gelatin has approximately the same elementary composition as the proteins, but is poorer in sulphur. A gelatin solution is lævorotatory. Gelatin solutions are precipitated by acetic acid and sodium chloride, or potassium ferrocyanide, the precipitate being soluble in excess of the latter: they are also precipitated by mercuric chloride and sodium chloride or hydrochloric acid, by metaphosphoric acid or phosphotungstic acid and hydrochloric acid, by potassium mercuric iodide and hydrochloric acid, or by saturation with ammonium sulphate.

Tannic acid precipitates a gelatin tannate from aqueous solution as a tough yellow precipitate. The gelatin-yielding substances (*collagen*) react similarly with tannic acid, and form leather. Gelatin solution give Millon's reaction and the biuret reaction: they give a weak xanthoproteic reaction.

When dry-distilled, gelatin yields pyrrole- and pyridine-bases (*bone oil*). Oxidation with permanganate yields oxamide (also obtained from other proteins) and guanidine (from arginine) (Ber. **38**, 455). By oxidation with acid hydrogen peroxide, acetone and *iso*valeraldehyde (probably derived from leucine) are obtained (C. 1902, II. 340).

Gelatin yields when hydrolysed with concentrated hydrochloric acid the same products as other proteins—glycine (about 16·5%), leucine, proline, hydroxyproline, serine, aspartic acid, glutamic acid, alanine, phenylalanine, arginine, etc. (E. Fischer, *loc. cit.*), but tyrosine and tryptophan are not obtained, and on putrefaction no phenol, indole or skatole are formed.

On more gentle treatment with hydrochloric acid there is formed the alcohol-soluble hydrochloride of gelatin-peptone. The behaviour of gelatin-peptone towards nitrous acid is indicative of the presence of primary and secondary, as well as tertiary, amino groups (Ber. **29**, 1084). Tryptic digestion of gelatin yields the diketopiperazine, prolylglycine anhydride (*cf.* Ber. **40**, 3544).

Although gelatin resembles in its general composition true protein, it is not capable of functioning as protein in animal metabolism, as certain essential amino-acids such as cystine and tryptophan are lacking.

By the accumulation of various special substances such as Ca and Mg or fat in collagen-containing tissues are formed bone, fatty tissue, cartilage, etc.

Elastin, which is distinguished from the true proteins by its low sulphur content, and which yields on hydrolysis glycine (25·75%), leucine (21·38%), alanine, phenylalanine, valune, proline and glutamic acid (C. 1904, I. 1364), belongs to this class, as does *keratin*, which forms the principal constituent of hair, nails, etc., and is distinguished by its high sulphur content (0·7–5%) (Ber. **28**, R. 561). Keratin yields much the same hydrolysis products as the proteins, including leucine, tyrosine, cystine, and serine (Ber. **35**, 2660). Elastin and keratin are more difficultly soluble and decomposed with greater difficulty than the genuine proteins. Elastin is attacked by pepsin and trypsin, while keratin is not. Various dipeptides such as *d*-alanyl-*l*-leucine, glycylvaline anhydride, *d*-alanylproline anhydride, are obtained by partial hydrolysis of elastin (Ber. **40**, 3544).

Fibroin, the principal constituent of silk, is allied to these substances. Silk also contains silk gelatin or *sericin*, which yields serine as its most important hydrolysis product. Fibroin is converted into a peptone-like compound when its solution in cold concentrated hydrochloric acid is allowed to stand, and from this peptone, trypsin liberates tyrosine. From the residue, which still resembles peptone, acids or alkalis produce glycine and alanine or glycylalanine (Chem. Ztg. **1902**, 940). A tetrapeptide of glycine, alanine and tyrosine has been isolated by partial hydrolysis of silk fibroin (Ber. **40**, 3552).

C. Conjugated Proteins

The conjugated proteins are more complex in their composition. By gentle acid hydrolysis they are split into a simple protein and a so-called *prosthetic group*, the latter including phosphoric acid, carbohydrate, nucleic acid or a coloured prosthetic group.

I. Glucoproteins

These yield on heating with mineral acids a protein and a sugar or amino-sugar. *Eichwald*, Ann. **134**: *Hofmeister*, Z. physiol. Chem. **24**, 169: *Müller* and *Seemann*, Deutsche med. Wochenschrift, **1899**, No. 13: *Seeman*, Arch. für Verdauungskrankheiten, IV, (1898).

Different types of glucoproteins include:

1. The *true glucoproteins* which are closely related to the true carbohydrate-free proteins. *Ovalbumin* in birds' eggs (*Hofmeister*, Z. physiol. Chem. **24**, 169)

is an example: it can be obtained crystalline, but of its uniformity there is doubt, and it probably contains mucoids (*q.v.*).

2. The *mucins* contain less carbon and nitrogen and more oxygen than the true glucoproteins, probably through a greater content of carbohydrate. They do not coagulate on heating in neutral or faintly alkaline solutions, and are not precipitated by acetic acid and potassium ferrocyanide and sodium chloride: they are thrown out of solution by excess of acetic acid. They form viscous, stringy solutions.

3. The *chondroproteins* are compounds of protein or gelatin with chondroitin-sulphuric acid (*q.v.*).

4. The *mucoids* (*mucinogens, hyalogens*) include a large number of little-investigated glucoproteins, *e.g. ovomucoid*, the *pseudomucin* of ovarian cysts, etc.

II. Phosphoproteins

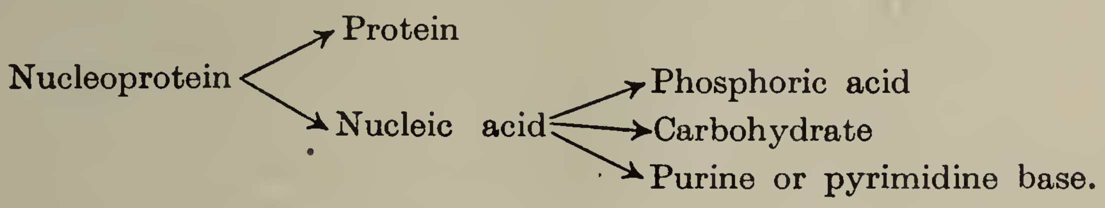
These are proteins in which phosphoric acid is chemically linked.

1. **Simple Phosphoproteins.**—Decomposed on heating with mineral acids into protein and phosphoric acid: insoluble in water, soluble in alkalis. Similar phosphoproteins can be obtained artificially from metaphosphoric acid and proteins (Pflüger's Arch. **47,** 155: Ber. **21,** 598).

Caseinogen (German, *Casein*), the most important protein constituent of milk, is a representative of this group. In its composition it resembles other proteins, but contains 0·85% phosphorus. It is contained in milk as a salt, and is precipitated by dilute acids as it is insoluble in water. It can be purified by dissolving in alkali and reprecipitating with acid. It can also be purified by the use of solid sodium chloride or magnesium sulphate, which precipitate it unaltered from solution. Among the hydrolysis products of caseinogen glycine is lacking, but tryptophan and tyrosine are abundant. Under special conditions, Fischer claims to have isolated a diaminotrihydroxydodecoic acid.

A solution of the alkali or calcium salt of caseinogen is not coagulated by heat. A calcium-free solution of caseinogen is not coagulated by rennet, but the addition of a calcium salt brings about coagulation, even if the rennin has been inactivated by heat. Rennin probably acts by splitting caseinogen into various proteins, including *casein* (German, *Paracasein*) which in the presence of calcium separates as a complex calcium salt (cheese manufacture).

2. **Nucleoproteins,** or **nucleins,** are appreciably more complex substances. Acid hydrolysis breaks them down into protein and so-called nucleic acid, which on more energetic hydrolysis can be broken down into phosphoric acid, carbohydrate and purine or pyrimidine bases.



The purine bases which occur are guanine and adenine: the pyrimidine bases, uracil, cytosine, thymine (*qq.v.*).

The nucleoproteins are the proteins of the cell nuclei and are obtained from tissues rich in nuclear material. They are obtained from spermatozoa, thymus gland, yeast, blood cells, etc. They are weak acids, and soluble, therefore, in alkalis, on which property their isolation is based. The proteins obtained by their hydrolysis are imperfectly investigated.

Nucleic Acids.—Preparation from *fish spermatozoa*, Z. physiol. Chem. **25**, 430 : from *thymus*, Ber. **27**, 2215 : from *yeast*, Z. physiol. Chem. **2**, 487 : from *wheat embryo*, Z. physiol. Chem. **36**, 85.

The products of partial hydrolysis of the nucleic acids are of importance in the study of their constitution (*Levene, Thannhauser*). On the one hand, purine or pyrimidine-carbohydrate compounds, the nucleosides, are obtained, *e.g.* adenosine, guanosine, cytidine, uridine (Ber. **41**, 27 : **42**, 43), and on the other hand, sugar-phosphoric esters, *e.g.* *d*-ribosephosphoric acid. From these products it is concluded that in the nucleic acids the sugar-phosphoric acid is linked in a glucosidic manner with the pyrimidine or purine base (in the latter, usually through *N*-atom 7, see purine, p. 637). Nucleosides have been obtained synthetically by the action of acetobromohexoses on purines or pyrimidines (Ber. **47**, 210, 1058, 1390, 1304).

III. Chromoproteins. (Hæmoglobins)

These conjugated proteins contain as their prosthetic group a coloured compound. The compounds of hæmochromogen with globins, the so-called hæmoglobins, are of particular importance.

Oxyhæmoglobin occurs in the red blood corpuscles and can be obtained crystalline from an aqueous solution of red blood cells, after the removal of cholesterol and lecithin by ether extraction, by cooling the solution after the addition of alcohol. The oxyhæmoglobins obtained from different animal species show differences, particularly in their crystalline form. The composition of oxyhæmoglobin differs from that of other proteins by the presence of 0·4% iron. If the molecular weight of hæmoglobin is calculated on the assumption that there is one atom of iron in the molecule, a value exceeding 13,000 is obtained (see also footnote, p. 743). The hæmoglobins form bright red crystalline powders, which are easily soluble in water and are reprecipitated in a crystalline form by the addition of alcohol. By evacuation of an aqueous solution of oxyhæmoglobin, or by the use of reducing agents (ammonium sulphide) oxygen is lost, and *hæmoglobin* (reduced hæmoglobin) formed ; the latter occurs in venous blood and can be obtained crystalline (Ber. **19**, 128). An aqueous solution of hæmoglobin rapidly takes up oxygen from the air and is reconverted into oxyhæmoglobin. Both compounds show in aqueous solution characteristic absorption spectra, by which they can readily be differentiated. (Preparation of crystalline oxyhæmoglobin from horse blood, and its conversion into hæmoglobin, see Z. physiol. Chem. **136**, 147.)

If carbon monoxide is passed into a solution of oxyhæmoglobin oxygen is displaced with the formation of *carbon-monoxide-hæmoglobin*, which can be obtained in large bluish crystals. This explains the toxicity of carbon monoxide. The solution of carbon-monoxide-hæmoglobin shows, like oxyhæmoglobin, two absorption bands between the Fraunhofer lines D and E, but unlike those of oxyhæmoglobin, they do not disappear on addition of ammonium sulphide.

Reduced hæmoglobin exhibits but one absorption band between D and E. Other gases, such as nitric oxide and hydrogen cyanide, are absorbed by hæmoglobin in equivalent amounts.

By the action of certain salts, such as nitrites, chlorates, permanganates, or of certain organic compounds, in particular of aniline, phenylhydroxylamine and quinone, oxyhæmoglobin is changed into methæmoglobin, which is differentiated from hæmoglobin by its absorption spectrum, and by the more stable combination with oxygen. Powerful reducing agents convert methæmoglobin into reduced hæmoglobin.

For the conversion of hæmoglobin into bile-pigments, see bilirubin, p. 753.

When warmed to 70° or by the action of acids or alkalis, oxyhæmoglobin is broken down into the protein *globin* and the pigment *hæmochromogen.*[*] A different globin is obtained from each animal species: hydrolysis of globin, see Fischer, *op. cit.*, pp. 695, 740. Hæmochromogen contains 9% iron and is converted by oxygen into hæmatin.

If oxyhæmoglobin (or dried blood) is warmed with a drop of glacial acetic acid and a little sodium chloride, microscopic red-brown crystals of *hæmin*, or *hæmatin chloride*, $C_{34}H_{30}N_4O_4FeCl$ (*Teichmann's crystals*), are produced (Ber. **29**, 2877 : **40**, 2021 : Ann. **358**, 213). By the action of alkali they yield *hæmatin*, $C_{34}H_{30}N_4O_4FeOH$. This reaction is used forensically as a delicate test for blood.

Hæmin.—On account of its ready crystallizability, hæmin has been thoroughly investigated. It contains four pyrrole nuclei. Only the more important aspects of the chemistry of blood pigments will be referred to here. Further information will be found in Vol. III at the end of the pyrrole compounds. Further references, *Abderhalden*, Handbuch der biolog. Arbeitsmethoden, Abt. 1. Teil. 8, Heft 2 : *H. Fischer*, Oppenheimer's Handbuch der Biochemie, 2. Aufl. Bd. I, 351 : Ber. **60**, 2611 : also the publications of *Willstätter*, *Küster*, *Piloty*, etc.

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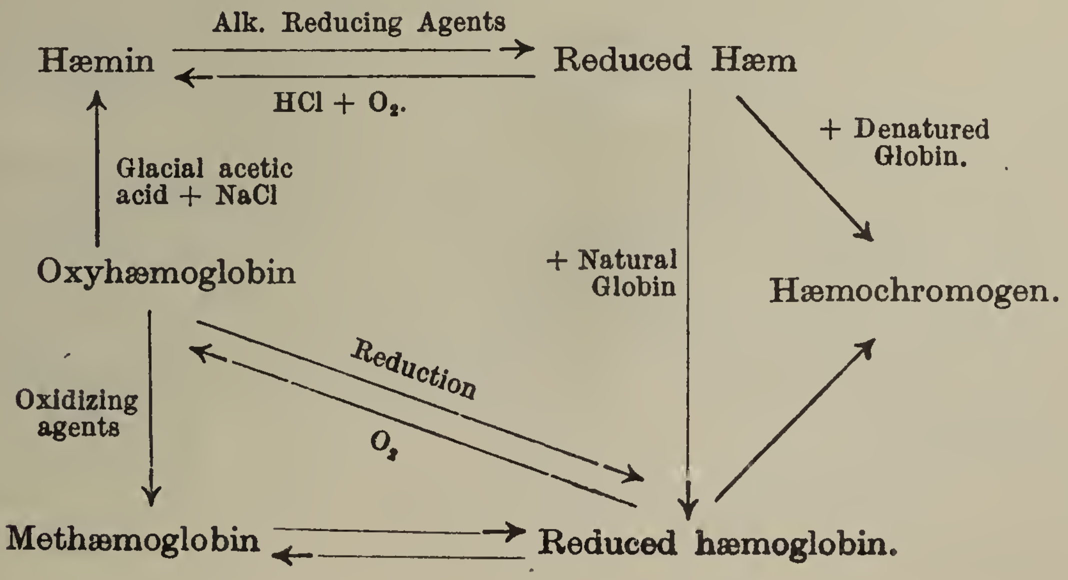
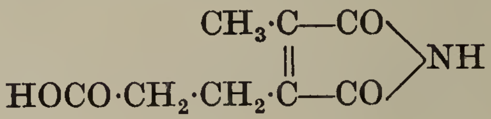
[*] According to recent work, hæmochromogen is not a protein-free pigment, but contains a pigment conjugated with denatured globin : the protein-free pigment is called *hæm*. Many other substances, such as pyridine, are capable of combining with hæm to form hæmochromogens. The relationships between some of the derivatives of hæmoglobin according to this scheme are given in the diagram below. (See *Anson* and *Mirsky*, J. physiol. 1925, **60**, 50, 161, 221 : J. Gen. Physiol. 1929, **13**, 121, 133, 469, 477 : *Barcroft*, Lecture, J.C.S. **1926**, 1146).



Hæmin is a dibasic acid, insoluble in indifferent organic solvents, soluble in alkalis, but insoluble in bicarbonate solutions. It forms a dimethyl ester and contains two unsaturated side chains, which can add on hydrogen or bromine.

Degradation of Hæmin.—1. *Oxidation* leads to the formation of *hæmatinic acid* (*Synthesis*), Ber. **47**, 582 : see also p. 648).



Hæmatinic acid is formed from the two pyrrole nuclei bearing carboxylic groups : the two bearing side chains are destroyed.

2. *Energetic reduction*, by hydrogen iodide and acetic acid, leads to a mixture of pyrroles and pyrrole carboxylic acids. The following have been obtained: (*a*) *Basic products. Hæmopyrrole,* 2 : 3-dimethyl-4-ethylpyrrole, *cryptopyrrole,* 2 : 4-dimethyl-3-ethylpyrrole, *phyllopyrrole,* 2 : 3 : 5-trimethyl-4-ethylpyrrole, and *opsopyrrole,* 3-methyl-4-ethylpyrrole. (*b*) *Acid products. Hæmopyrrolecarboxylic acid,* 2 : 3-dimethylpyrryl-4-propionic acid, *cryptopyrrolecarboxylic acid,* 2 : 4-dimethylpyrryl-3-propionic acid, *phyllopyrrolecarboxylic acid,* 2 : 3 : 5-trimethylpyrryl-4-propionic acid.

3. Less energetic reduction leads to the metal-free *porphyrins,* first obtained by Hoppe-Seyler and Nencki, which contain the skeleton of hæmin practically unaltered. Acetic acid and hydrogen bromide convert hæmin into the long-known crystalline *hæmatoporphyrin,* $C_{34}H_{34}N_4O_4(OH)_2$, which forms salts with dilute acids or alkalis, also esters and ethers. Hydrogen iodide and glacial acetic acid yield *mesoporphyrin,* $C_{34}H_{38}N_4O_4$, which forms a hydrochloride, alkali salts and esters. In the latter both unsaturated side chains have been hydrogenated, and an additional product obtained by the oxidative breakdown of this compound is methylethylmaleinimide (*Synthesis*, Ann. **345**, **11**). Further reduction of mesoporphyrin with potassium amalgam yields *mesoporphyrinogen,* $C_{34}H_{44}O_4N_4$, the leuco-derivative of mesoporphyrin. *Hæmoporphyrin,* which is formed from hæmatoporphyrin by the action of methyl-alcoholic potash at high temperatures, and which on loss of its carboxyl groups yields ætioporphyrin III,* is probably isomeric with mesoporphyrin. Ætioporphyrin is obtained from chlorophyll, and this reaction shows the close relationship of the two biologically most important pigments.

Natural Porphyrins.—Under pathological conditions (*porphyrinuria*) the urine contains considerable quantities of *uroporphyrin* and *coproporphyrin* (Z. physiol. Chem. **95**, 34 : **96**, 148, 309 : **97**, 109, 148 : **98**, 14, 78). Both these porphyrins are derived from ætioporphyrin I, uroporphyrin containing eight, and coproporphyrin four carboxyl groups. Coproporphyrin can be demonstrated spectroscopically in the fæces of vegetarians, and has been isolated from yeast (Z. physiol. Chem. **138**, 55). *Turacin,* a pigment in the feathers of the turacus bird, is the copper salt of uroporphyrin.

Other porphyrins related to blood pigment occur in nature. In the pigmented shell of wild birds (particularly sea-gulls) *ooporphyrin* is found (Z. physiol. Chem. **131**, 241 : **138**, 262). Ooporphyrin (*protoporphyrin, Kammerer's porphyrin*), like hæmin, from which it can be obtained by the removal of iron, contains two carboxyl groups. The putrefaction of blood produces *deuteroporphyrin,* $C_{30}H_{30}N_4O_4$, which on oxidation yields citraconimide and hæmatinic acid : in this compound, both unsaturated side chains have been split off.

The porphyrins mentioned above are distinguished by a characteristic absorption spectrum and by their capacity to form complex iron derivatives.

Many other porphyrins, which do not occur in nature (up to 1928 about 30 different) have been obtained synthetically. Summary, H. Fischer, Ber. **60**, 2611. The methods employed will be dealt with in Vol. III under pyrrole.

The relationships between the various compounds dealt with is given in the following diagram :

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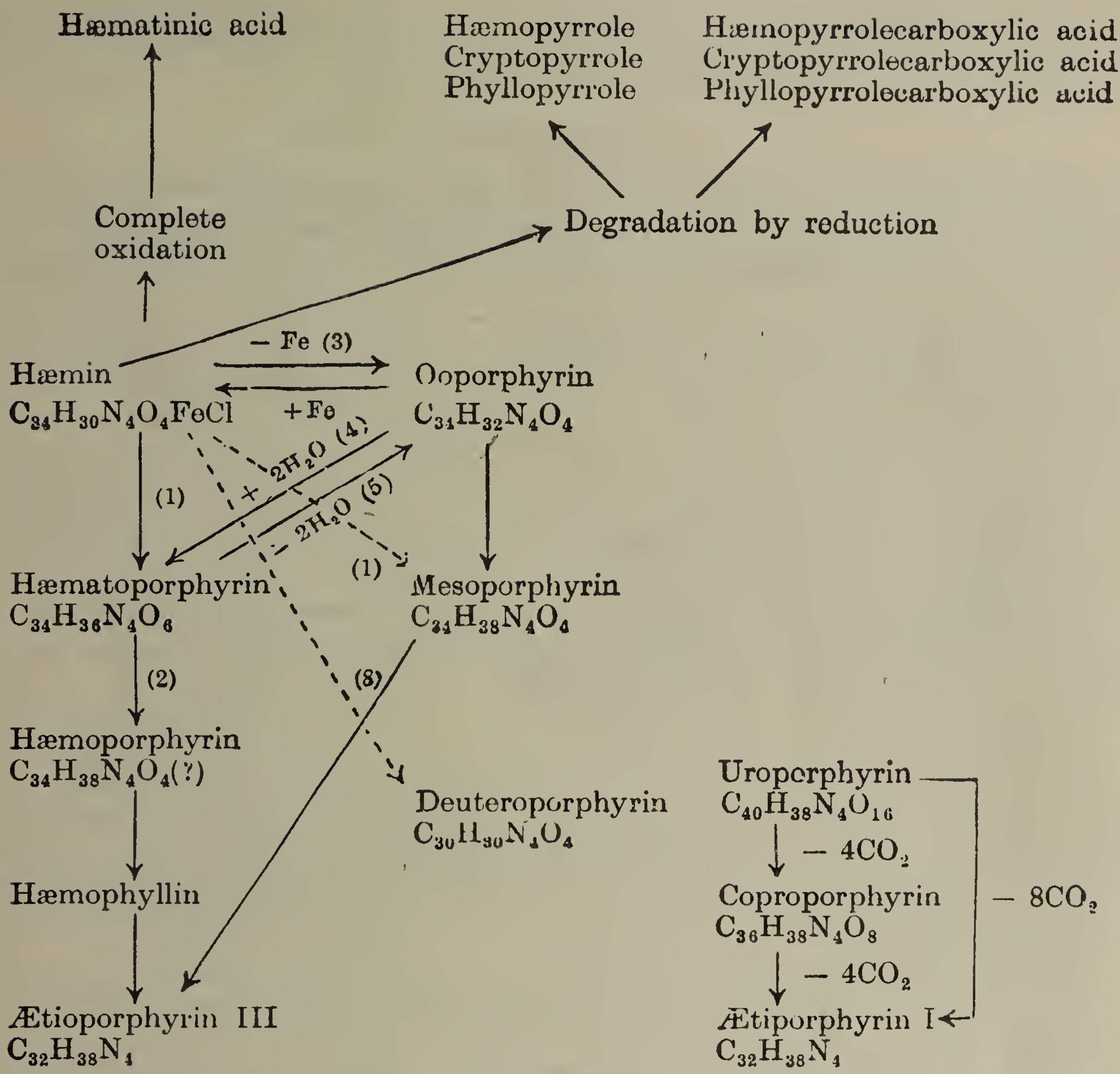
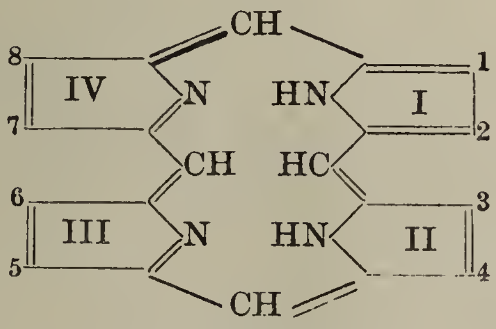
* Meaning of the roman numeral, see Ann. **459**, 54 ; also p. 751.



References to above scheme : (1) Ber. **34**, 997. (2)–(8), all Z. physiol. Chem. (2) **87**, 423. (3) **154**, 39. (4) **142**, 156. (5) **142**, 142. (6) **140**, 241. (7) **138**, 49. (8) **140**, 231 : **161**, 18.

Constitution.—From the results of molecular weight determinations and of synthetic and analytical experiments, it appears that all porphyrins and the hæmins and phyllins obtained from them by the introduction of iron or magnesium contain a so-called *porphin nucleus* (Ber. **60**, 2639), for which the structure suggested by W. Küster (Z. physiol. Chem. **82**, 463), consisting of four pyrrole residues linked by methine groups in the α-positions, expresses the findings most satisfactorily.



Porphin-skeleton.

It will be noticed that I is a genuine pyrrole ring, whereas III and IV are pyrrolenine rings and II the ring of maleinimide. By the introduction of methyl, ethyl and propionic acid groups on the carbon atoms 1–8, the numerous porphyrins are obtained, likewise four ætioporphyrins, all of which have been synthesized (Ann. **459**, 53). Of these ætioporphyrins, *ætioporphyrin I*, 1 : 3 : 5 : 7-tetramethyl-2 : 4 : 6 : 8-tetraethylporphin, is of importance from its relationship to uro- and coproporphyrins, while *ætioporphyrin III*, 1 : 3 : 5 : 8-tetramethyl-

2 : 4 : 6 : 7-tetraethylporphin, is the basis of hæmin and of oo- and meso- and the other porphyrins obtained from blood pigment. Mesoporphyrin is 1 : 3 : 5 : 8-tetramethyl-2 : 4-diethylporphin-6 : 7-dipropionic acid.

Chlorophyll

By this name are referred to the plant pigments which occur in all green plants, and which are of importance physiologically to the plant, and also indirectly to animals in connection with natural synthetic processes.

It is noteworthy that chlorophyll, the green plant pigment, and hæmin are related, at any rate in their breakdown products (see p. 750). Just as hæmin is peculiar in its iron content, so chlorophyll is characterized by its content of magnesium (*Willstätter*).

Amorphous chlorophyll can be obtained from fresh or dried plants by extraction with alcohol : the extract can be purified by extraction with benzene or carbon bisulphide and water.

The pigment thus obtained is a mixture of 3 parts chlorophyll *a*, $C_{55}H_{72}O_5N_4Mg$, and 1 part chlorophyll *b*, $C_{55}H_{70}O_6N_4Mg$ (Ann. **380**, 177 : *separation*, see Ann. **390**, 294).

Chlorophyll a contains two carboxyl groups, of which one is esterified with methyl alcohol, the other with the unsaturated alcohol phytol (see p. 152). The existence of a third carboxyl group, probably in the form of a lactam ring, is uncertain. From these facts, the formula of chlorophyll *a* (with suitable modification for chlorophyll *b*) can be written $(C_{32}H_{30}ON_4Mg)COOCH_3{\cdot}COOC_{20}H_{39}$. Chlorophyll *a* and *b* are closely related, and their breakdown leads finally to identical products.

The oxidative degradation of chlorophyll products with lead peroxide and sulphuric acid or chromic acid yields hæmatinic acid (p. 750) and methylethylmaleinimide (Ann. **373**, 227).

Energetic reduction with tin and hydrochloric acid or glacial acetic acid and hydrogen iodide (Ann. **385**, 188) yields hæmopyrrole and phyllopyrrole (p. 750).

Acids remove magnesium from chlorophyll with the formation of *phæophytin*, $(C_{32}H_{32}ON_4)COOCH_3{\cdot}COOC_{20}H_{39}$. The corresponding free dicarboxylic acid is phytochlorin *e* : the introduction of magnesium leads to the formation of a *phyllin*. Alkalis hydrolyse the ester groups, without touching the magnesium-containing nucleus. According to the conditions the products are *chlorophyllin*, $(C_{32}H_{30}ON_4Mg)(COOH)_2$, or the isomeric iso*chlorophyllin*. Progressive decarboxylation leads through a series of other phyllins eventually to the oxygen-free *ætiophyllin*, $C_{31}H_{34}N_4Mg$, from which dilute acids produce ætioporphyrin (Ann. **400**, 182).

Other Plant Pigments

A number of yellow and red, chemically indifferent pigments accompany chlorophyll. They can be divided into two groups, (*a*) the oxygen-free carotinoids and (*b*) the oxygen-containing xanthophylls. Both classes give an indigo-blue colour with concentrated sulphuric acid and are oxidized in air.

(*a*) **Carotinoids** (see also p. 118).—*Carotene*, $C_{40}H_{56}$, m.p. 156°, forms reddish-yellow crystals and is obtained from carrots (*Daucus carota*) (Ann. **355**, 8 : Z. physiol. Chem. **64**, 47), from *corpus luteum* (Z. physiol. Chem. **83**, 198) and from *gall stones* of oxen (Z. physiol. Chem. **88**, 331). It can be hydrogenated catalytically (Ber. **61**, 566). *Triiodide*, $C_{40}H_{56}I_3$, m.p. 137°, forms deep-violet, whetstone-shaped crystals. *Lycopene*, $C_{40}H_{56}$, m.p. 168–9°, the pigment of tomatoes, is isomeric with carotene (Z. physiol. Chem. **64**, 47) and yields with iodine amorphous products.

(*b*) **Xanthophylls.**—*Xanthophyll* (*a*), $C_{40}H_{56}O_2$, m.p. 172°, forms yellow crystals. An isomer is the ovarian pigment *lutein*, m.p. 193°, also known as *xanthophyll* (*b*) (Z. physiol. Chem. **76**, 214). *Fucoxanthin*, $C_{40}H_{54}O_6$, is obtained from brown seaweeds, and forms brown-red prisms, + $3CH_3OH$, m.p. (dried) 160° (Ann. **404**, 237). Summary, see *R. Willstätter*, Ber. **47**, 2831.

Bile Pigments and Bile Acids

In the bile, the secretion of the liver, which is indispensable for the digestion of fats, occur the bile pigments and a series of acids, the most important of which are glycocholic and taurocholic acids: the bile also contains lecithin and cholesterol.

Bilirubin, $C_{33}H_{36}N_4O_6$, is the most important of the bile pigments. It is obtained from gall-stones in the form of brownish-yellow crystals (Z. physiol. Chem. **73**, 216) and, like hæmin, is a dibasic acid, which forms a well-crystallized ammonium salt and esters. Bilirubin is formed in the body from blood pigment. This is not confined to the liver, but occurs throughout the so-called reticulo-endothelial system of the body, which is distributed principally in the spleen, bone-marrow and liver. It has long been known that in old extravasations of blood beautiful brownish-yellow crystals occur, which were referred to as *hæmatoidin*. Fischer and Reindel have shown that hæmatoidin is identical with bilirubin (Z. physiol. Chem. **127**, 299).

Oxidation of bilirubin yields hæmatinic acid (p. 750). Bilirubin is more stable towards reducing agents than hæmatin, and an intermediate product containing two pyrrole nuclei, *bilirubinic acid* (m.p. 187°), can be isolated, whose constitution has been elucidated by Hans Fischer (see Vol. III). More complete degradation leads to the formation of cryptopyrrole and cryptopyrrolecarboxylic acid.

Bilirubin can be catalytically hydrogenated to *mesobilirubin*, $C_{33}H_{40}N_4O_6$, m.p. 315°. Sodium amalgam reduces it to the leuco-compound *mesobilirubinogen*, m.p. 203°, which on oxidation yields mesobilirubin. Oxidation by air produces from mesobilirubinogen urobilin, which occurs in the fæces and to a small amount in normal urine, but whose constitution is uncertain.

The Bile Acids.—The three bile acids which to date have been obtained from ox gall-stones can be referred to a common cholanic acid, $C_{24}H_{40}O_2$, as basis. The known bile acids are hydroxy derivatives of this acid.

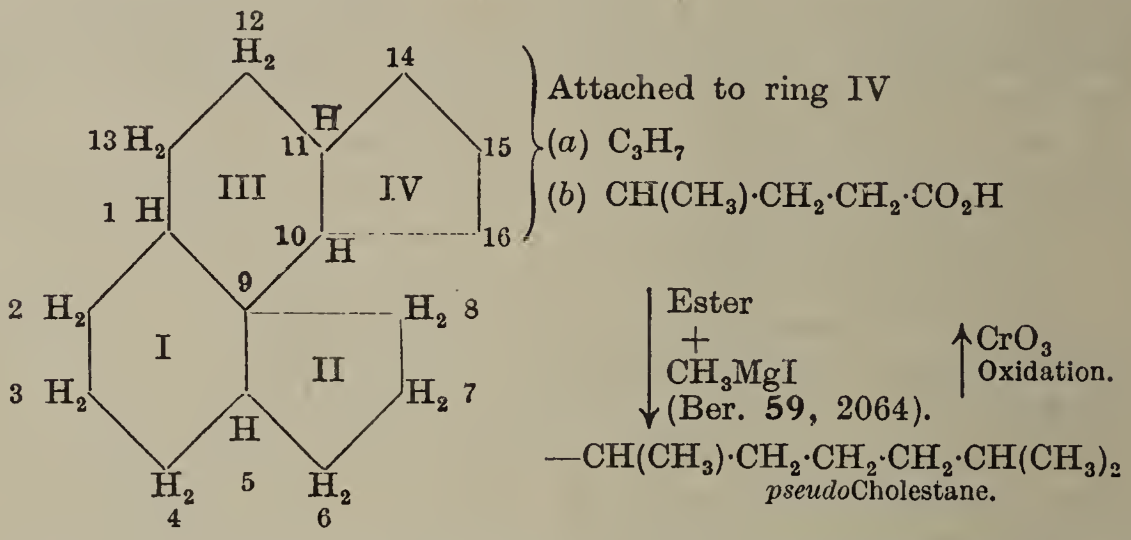
1. *Lithocholic acid*, 3-hydroxycholanic acid, $C_{24}H_{40}O_3$, m.p. 186° (Z. physiol. Chem. **73**, 234 : **110**, 123).
2. *Desoxycholic acid*, 3 : 7-dihydroxycholanic acid, $C_{24}H_{40}O_4$, m.p. 172° (Z. physiol. Chem. **97**, 1 : **98**, 59).
3. *Cholic acid*, 3 : 7 : 12-trihydroxycholanic acid, $C_{24}H_{40}O_5$, m.p. 195° (Z. physiol. Chem. **80**, 297).

The above three acids all occur in ox gall.

4. *Hyodesoxycholic acid*, 3 : 13-dihydroxycholanic acid, m.p. 196–197°, isomeric with desoxycholic acid, occurs in the bile of swine (Ann. **433**, 282 : **447**, 233).
5. *Cheno-* or *Anthropodesoxycholic acid*, 3 : 12-dihydroxycholanic acid, m.p. 140° (solvent-free), is obtained from human (Z. physiol. Chem. **140**, 186) or goose (Z. physiol. Chem. **140**, 167) bile. *Constitution*, see Z. physiol. Chem. **157**, 180.

In bile those acids are conjugated with glycine or taurine, *e.g.*, to glycocholic acid, $C_{24}H_{39}O_4{\cdot}NH{\cdot}CH_2{\cdot}CO_2H$, m.p. 133°, and taurocholic acid, $C_{24}H_{39}O_4{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}SO_3H$, m.p. indef., which can be decomposed into their constituents by prolonged boiling with alkali.

The constitution of the bile acids has been largely elucidated by the work of Wieland and his school. The skeleton of the bile acids, as of cholesterol, is a tetracyclic fully hydrogenated ring structure (see below) which contains attached to ring IV a side chain of known structure, and three carbon atoms whose distribution is uncertain (see *Wieland,* Z. physiol. Chem. 1912–1924 : degradation of side chain, *ibid.* **161**, 80). The apparent relationship of the bile acids to the sterols is demonstrated by the oxidation of *pseudo*cholestane to cholanic acid (*Windaus*, Z. physiol. Chem. **100**, 167). The oxidation of cholestane proceeds similarly with formation of allocholanic acid. The structure of the fundamental cholanic acid and its relation to the sterols is shown in the following scheme :



Desoxycholic acid forms well-defined crystalline addition products with fatty acids and other organic compounds, *e.g.*, 1-*desoxycholic acid*-8-*palmitic acid,* m.p. 186°, once called choleic acid. This combination of fatty acids with desoxycholic acid is of physiological importance. *Dehydrocholic acid* (3 : 7 : 12-triketocholanic acid) is used therapeutically as a cholagogue under the name decholin.

Sterols

The sterols occur both free and combined as esters of higher fatty acids both in the animal and vegetable kingdoms. The sterols give certain group reactions, *e.g.*, a deep-red to bluish-red colour when their chloroform solutions are treated with concentrated sulphuric acid (*Salkowsky's test*). Another characteristic is the ability of the majority of sterols to combine with saponins, especially digitonin, to give sparingly soluble molecular compounds which can be used for the quantitative estimation of free sterols (*Windaus*, Ber. **42**, 238).

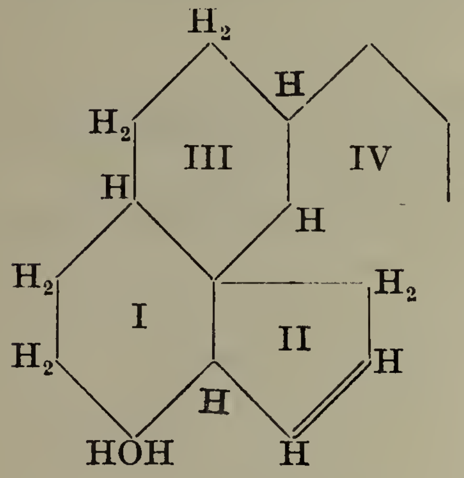
Cholesterol, $C_{27}H_{45}OH$, is the most important zoosterol (sterol of animal origin). It has m.p. 148°, b.p. *c.* 360°, $[\alpha]_D - 37{\cdot}8°$ (in ether). In addition to its occurrence in bile (*χολη*, bile, *στεαϱ*, fat : gall-stones contain up to more than 90% cholesterol), cholesterol occurs in the brain, in blood, in yolk of egg, etc.

It is insoluble in water, but soluble in the majority of organic solvents : from alcohol it crystallizes in mother-of-pearl plates or tables with a soapy feel, containing $1H_2O$; from ether it crystallizes anhydrous in needles.

It protects the red blood cells against hæmolysis, by certain toxins, and has therefore an antitoxic action (C. 1905, I. 1265 : Ber. **42**, 238).

For our knowledge of the constitution of cholesterol we are indebted to Mauthner, Suida, Diels and particularly to Windaus. It is a cyclic secondary alcohol containing a double bond, derived from the saturated hydrocarbon cholestane, m.p. 81°. As the corresponding open-chain saturated hydrocarbon would have the formula $C_{27}H_{56}$, the 8 hydrogen atoms less of cholestane suggest a tetracyclic hydrogenated ring system.

Two rings have been established by systematic degradation. Ring I which contains the hydroxyl group is a 6-membered ring, while ring II which contains the double bond is a 5- ring. The conversion of *pseudo*cholestane into cholanic acid (above) is evidence that the remaining two rings are identical with those of the bile acids. Cholesterol and the bile acids are distinguished, apart from their spatial configuration, by an *iso*propyl group in the side chain. The present state of our knowledge of cholesterol constitution is given in the following formula:



Attached to ring IV
(*a*) C_3H_7
(*b*) $-CH(CH_3){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH(CH_3)_2$

Cholesterol.

In the gut cholesterol is reduced to the saturated alcohol *coprosterol*, $C_{27}H_{48}O$, m.p. 112°, $[\alpha]_D + 24°$. This reduction can be achieved chemically (Ann. **453**, 101). Coprosterol is actually not the normal dihydrocholesterol, but is derived from a stereoisomeric hydrocarbon, *pseudo*cholestane (*coprostane*, $C_{27}H_{48}$, m.p. 78–79°) (Monatsh. **30**, 639), which is the connecting-link with the bile acids (see p. 753 and Z. physiol. Chem. **100**, 167).

The esters of cholesterol and of *iso*cholesterol with higher fatty acids form lanolin (wool-fat) which occurs in raw wool and is used as a basis for ointments, as it is taken up by the skin.

Phytosterols.—The vegetable sterols or phytosterols are widely distributed. Some are isomeric with cholesterol, but others contain more than one double linking. *Sitosterol*, $C_{27}H_{46}O$, m.p. 137°, $[\alpha]_D - 33{\cdot}9°$ (Ber. **39**, 4378: **40**, 3681), is the most important sterol of the higher plants and is obtained from wheat seedlings or calabar beans. *Stigmasterol*, $C_{30}H_{48 \text{ or } 50}O$, H_2O, m.p. 170° $[\alpha]_D - 45°$ (chloroform) (Ber. **39**, 4378), occurs with sitosterol in the calabar bean and contains two double bonds. *Brassicasterol*, $C_{28}H_{46}O$, m.p. 148° (Ber. **42**, 614), from rape oil. *Ergosterol*, $C_{27}H_{43}O$, H_2O, m.p. 165°, $[\alpha]_D - 132°$ (chloroform) (C. 1908, II. 716: Ann. **452**, 34: **460**, 212), occurs with *fungisterol*, $C_{25}H_{40}O$, H_2O, m.p. 144°, in ergot of rye: it is best obtained from yeast fat or from yeast (Z. physiol. Chem. **124**, 8: Ann. **460**, 218). Ergosterol is the typical sterol of the cryptogams and contains three double bonds. Irradiation with ultra-violet light produces the anti-rachitic vitamin D. This anti-rachitic vitamin has recently been obtained crystalline and is called *calciferol* (Proc. Roy. Soc. 1931, [B], **108**, 340).

Enzymes *

It has long been known that certain reactions were accelerated or catalysed by substances of unknown constitution occurring both in plant and animal tissues, *e.g.*, formation of maltose from starch, inversion of sucrose, hydrolysis of amygdalin. These organic or biological catalysts, which also act when separated from living cells, are known as enzymes.

The isolation of an enzyme in absolutely pure condition has not yet been achieved: methods have, however, been evolved by which enzyme preparations of great activity are obtained. The preparation usually involves the two stages:

(i) Extraction of the crude enzyme from the animal or plant tissue by pressing-out or by the action of solvents.

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* *H. v. Euler*, Chemie der Enzyme: *C. Oppenheimer*, Fermente und ihre Wirkungen, Leipzig, 1924, Thieme: *H. v. Euler*, Lecture, Ber. **55**, 3582: *R. Willstätter*, Ber. **55**, 3601: **59**, 1: Naturwissenschaften, **15**, 585: *P. Rona*, Praktikum der physiologischen Chemie, Teil 1, Fermentmethoden, Berlin, 1926, Springer: *E. Waldschmidt-Leitz*, Die Enzyme, Braunschweig, 1926, Vieweg.

(ii) The concentration of the enzyme by the following methods:

(*a*) The removal of admixed substances by the salting-out action of metallic salts.

(*b*) Precipitation with alcohol.

(*c*) Adsorption of the enzyme on a colloid with the opposite electric charge (iron hydroxide, aluminium hydroxide, kaolin) followed by the removal (*elution*) from the adsorbent.

Willstätter and his colleagues in particular have developed methods for the concentration of enzymes based on adsorption and elution (Z. physiol. Chem. **125,** 93: Ann. **425,** 1). By these methods, for example, invertin, the enzyme which hydrolyses cane-sugar, has been concentrated 12,000 times and pancreatic lipase 300 times, at the same time being freed from accompanying enzymes. The increasing instability of enzymes with increasing purity has hindered the attempts to obtain them quite pure.

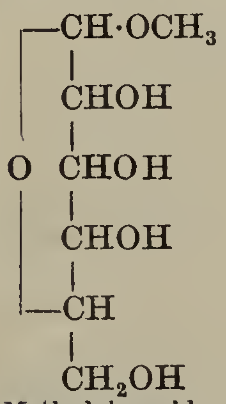
According to Willstätter, the enzymes consist of a colloidal carrier and a purely chemically-acting active group. They cannot be placed in any of the hitherto known classes of natural products.

Enzymes are named after the substrates which they break down:
Fat-hydrolysing enzymes, *Lipases, e.g.* Pancreatic lipase.
Protein-hydrolysing enzymes, *Proteases, e.g.* Trypsin, Erepsin, Pepsin.
Cane-sugar-hydrolysing enzymes, *Saccharases, e.g.* Invertin (Invertase) of yeast.
Starch-hydrolysing enzymes, *Amylases, e.g.*, Malt amylase or diastase.
Glucoside-splitting enzymes, *Glucosidases, e.g.* β-Glucosidase in emulsin.
Dehydrogenating enzymes, *Oxidases* and *peroxidases.*
Reducing enzymes, *Reductases.*
Enzymes which remove CO_2, *Decarboxylases.*
Enzymes which remove sulphuric acid, *Sulphatases.*

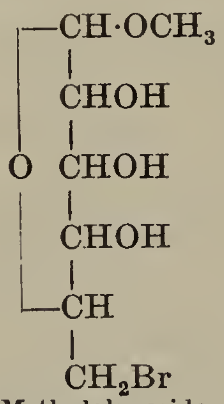
Enzymes are also known which have a synthetic action, with the formation of C—C links. These are known as *carboligases* (*Neuberg,* Ber. **55,** 3635: *cf. Lintner* and *Liebig,* Z. physiol. Chem. **88,** 109). For examples of enzymatic synthesis of disaccharides, see the end of this section.

A typical property of the enzymes, which distinguishes them from the inorganic catalysts, is their extraordinary specificity, *i.e.*, the property which restricts their action to a very definite substrate. The relation between enzyme action and substrate constitution, which has been likened by E. Fischer to a key (enzyme) and lock (substrate), is abundantly confirmed experimentally.

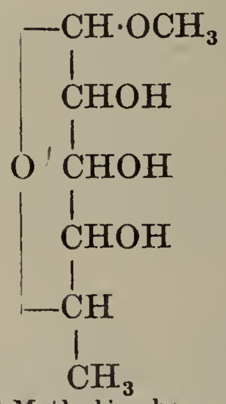
For the study of this problem the glucosides are well suited. A typical example of enzyme specificity is given by the action of emulsin β-glucosidase on the aqueous solutions of the following β-glycosides:



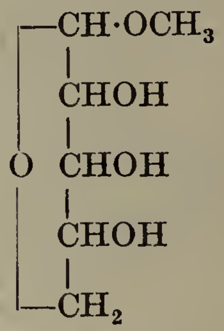
β-Methylglucoside. Hydrolysed.



β-Methylglucoside-6-bromohydrin. Not hydrolysed.



β-Methyl*iso*rhamnoside. Hydrolysed.



β-Methylxyloside. Not hydrolysed.

None of the above glycosides are attacked by the enzymes of bottom-yeast, which contains only α-glucosidase.

The activity of enzymes is profoundly influenced by the presence of electrolytes and other substances.

1. *Hydrogen Ion Concentration,* p_H.—Many enzymes have their optimum activity at a definite, usually very weakly acid reaction. Following Sørensen the hydrogen ion can be represented by the calculation of the normality of a solution as an exponent to the base 10, the negative sign being neglected, *e.g.*:

$$N/100 \text{ acid} = 10^{-2} : \; p_H = 2{\cdot}0$$
$$N/10000 \text{ acid} = 10^{-4} : \; p_H = 4{\cdot}0$$

For $N/500$ acid the p_H is calculated as follows:

$$0{\cdot}002 = 2 \times 10^{-3} = \text{(say) } 10^x$$
$$\log 2 - 3 = x$$
$$\text{i.e. } x = -2{\cdot}7$$
$$\therefore\; p_H = 2{\cdot}7.$$

For the maintenance of a definite hydrogen ion concentration, so-called buffers are used. These are acid-salt mixtures which only change their reaction slightly when acid or alkali is added to their solutions, and the hydrogen ion concentration is thus maintained nearly constant throughout the reaction. Such buffer mixtures consist of sodium acetate + acetic acid, the sodium phosphates NaH_2PO_4 and Na_2HPO_4 (Michaelis), sodium citrate + hydrochloric acid, sodium citrate + sodium hydroxide (Sørensen).

The optimal hydrogen ion concentrations for certain important enzymes are given in the following table:

Enzyme.	*Optimum* p_H.	*Source of enzyme.*
Amylase	6·7	Pancreas
Saccharase	4·4–4·6	Yeast
Maltase	6·6	Beer-yeast
α-Glucosidase	5·8–6·6	Bottom yeasts
β-Glucosidase	5	Emulsin
Pepsin	1·6–1·8	Gastric juice
Catalase	7	Liver

2. Enzyme action is influenced by the *presence of other ions. E.g.* Pancreatic amylase depends upon the presence of chlorine ions, trypsin is markedly influenced by calcium ions.

3. *Temperature.*—Every enzyme has a maximum activity at a definite temperature. In general this lies between 37° and 53°. Higher temperatures rapidly produce inactivation.

4. *The Presence of Coenzymes.*—Many organs yield their enzyme in an inactive form, the so-called *zymogens,* which are only made active by certain other substances or *coenzymes* (Kinases).

A typical example of this is the activation of the vegetable protease papain by hydrogen cyanide (*Willstätter* and *Grassmann,* Z. physiol. Chem. **138**, 184). The system papain-hydrogen cyanide has an altogether different working range from that of papain alone. The proteolytic enzyme of the pancreas, trypsin, requires the presence of a coenzyme obtained from the intestinal wall, so-called enterokinase, for certain of its activities (Z. physiol. Chem. **132**, 181 : **149**, 203).

5. *Inhibition and Poisoning of Enzymes.*—Heavy metal salts in particular prevent the action of enzymes. Among organic compounds chloroform, toluene, and bases such as aniline and phenylhydrazine have an inhibitory effect.

The action of enzymes is pictured as due to the combination of the enzyme with its substrate, the complex formed then breaking down into other products. The action of yeast saccharase on cane sugar is illustrated as follows:

Cane sugar + saccharase = [Cane-sugar · saccharase] = Glucose + fructose + saccharase.

The speed of such a hydrolytic process is then dependent upon (1) the speed of formation and (2) the speed of decomposition of the [cane-sugar · saccharase] complex. The law of mass action holds for both stages.

Euler has postulated the existence of carbonyl groups in the intestinal peptidases (*e.g.* erepsin) as the enzyme activity is prevented by aldehyde reagents such as aniline and phenylhydrazine, probably because of blockage of the active group which combines with the substrate (Z. physiol. Chem. **162**, 85).

Enzymatic Syntheses.—Detailed study of enzyme hydrolysis shows that the hydrolysis does not proceed to completion, but an equilibrium is established. The predicted property of enzymes to work synthetically (van 't Hoff) has been widely confirmed. Investigations have largely been carried out in the realm of the disaccharides (Bourquelot, Pringsheim).

Enzymatically Synthesized Disaccharides

Enzyme.	*Substrate.*	*Duration of action.*	*Product of synthesis.*	*References.*
Yeast maltase	Glucose	Several months	*iso*Maltose and dextrins	C. 1898, II. 632 : Ber. **34**, 600
Purified yeast maltase	40% Glucose (p_H 6·4)	1 month 37°	Maltose	Ber. **57**, 1576
Kefir lactase	Galactose + glucose	15 days	*iso*Lactose	Ber. **35**, 3144
Emulsin . .	5% Glucose	1 month	Gentiobiose	Compt. rend. **157**, 732
Emulsin . .	50% Glucose	1 month	Cellobiose	Compt. rend. **168**, 1016
Emulsin . .	Galactose	5 months	Galactobioses A and B	Compt. rend. **164**, 443

The union of glucose and fructose to cane sugar has not yet been achieved. In addition to the above syntheses, syntheses of higher carbohydrates, fats, and proteinoid substances have been successfully carried out. Neuberg has brought about syntheses involving a C—C link by the carboligase of yeast (Ber. **55**, 3636).

INDEX

Individual substances should also be sought under the more general headings: in particular, derivatives of acids such as esters, amides, nitriles are not indexed separately where their description in the text follows immediately on that of the parent substance, and the same applies to oximes and phenylhydrazones of many ketonic substances, and to the acetals of many aldehydes.

END OF VOLUME I